ARCHIVES OF OPHTHALMOLOGY

VOLUME 25 (old series Volume 82) MARCH 1941 NUMBER 3

COPYRIGHT, 1941, BY THE AMERICAN MEDICAL ASSOCIATION

SOME OCULAR PHENOMENA PRODUCED WITH POLARIZED LIGHT

DAVID G. COGAN, M.D.

BOSTON

Interest in polarized light has increased during the past few years owing to the fact that inexpensive, large area polarizing materials have become available. A new material, which bears the trade name polaroid, is suitable for incorporation in optical systems and is, in fact, already standard equipment for use with some ophthalmoscopes. It seems appropriate, therefore, to describe and discuss at this time certain ocular phenomena that I have observed with polaroids.

The phenomena are of two types: One is produced by the lens of the eye and has previously been described in part; the other is produced by the anterior segment of the intact eye and has not, to my knowledge, previously been noted in the literature. Both are produced by crossed polaroids and have in common the appearance of a black cross on a bright background, but as I have no right at the outset to assume that the same explanation is applicable to both, I shall discuss them separately.

CROSS PRODUCED BY THE LENS

A satisfactory and simple way of observing this phenomenon is as follows: The lens is removed from the eye and placed in a dish containing fluid or saline solution, and the dish is placed between two polaroids over an incandescent lamp. The observer looks through the dish from above. The polaroid between the light source and the dish is called the polarizing polaroid and that between the dish and the observer the analyzing polaroid. By rotating the analyzer until its axis is at right angles to that of the polarizer, most of the field will become dark, but not that portion of the field containing the lens. The lens stands out conspicuously, as seen in the figure, *A*. The four quadrants of the lens stand out brightly but are separated by two lines forming a dark cross. At the periphery of the lens there is also a dark ring separating an outermost luminous fringe from the rest of the lens. The

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

arms of the cross are 1 to 2 mm. wide and of equal breadth throughout, except perhaps at their intersection, where they are slightly wider. The demarcation of the arms from the luminous quadrants is not distinct.

The arms of the cross correspond to the axes of the polaroids. When the analyzer, or polarizer, is separately moved, the cross appears to rotate with the rotation of the polaroid for 5 to 10 degrees before disappearing. As the polaroid is further rotated, the lens becomes almost uniformly luminous along with the rest of the field. There are, however, four small shadow-like areas of diminished luminosity at the extreme periphery that rotate with the polaroid and do not disappear. They appear to be the peripheral tips of the arms of the cross. It is as though the tips of the cross do not disappear when the polaroid is turned but continue to rotate around the periphery of the lens and ultimately merge, when a new cross is formed, with the arms at right angles to those from which the tips appeared to originate. As the cross is visible only when the axes of the polarizer and analyzer are approximately at right angles to each other, the cross, on rotation of the polaroid, is seen only at rotating intervals of 180 degrees. It is interesting, however, that the peripheral shadow-like areas which I have mentioned move only 90 degrees when the polaroid is rotated 180 degrees.

When both polaroids are rotated equally and simultaneously, the dark areas that are visible at the start of the rotation will rotate with the polaroids and show no change in form. Thus, if the polaroids are at right angles to each other to begin with, the cross so produced will rotate with the polaroids and remain intact.

Two polaroids are employed in the production of the phenomenon. When either analyzer or polarizer alone is used, the appearance of the lens is the same as that without polaroids, except for slight diminution in intensity.

The first reported examination of the crystalline lens by means of polarized light was, so far as I am aware, that of David Brewster[1] in 1815. Brewster examined with Nicol prisms a variety of substances as widely different as mother-of-pearl and cow's bladder. Among his comments on the various tissues he stated: "The tunica retina and the crystalline lens exercise no peculiar action on (polarized) light." Although he apparently did not observe the lenticular cross, he did describe a cross in oil of mace.

The lenticular cross was apparently first described by von Erlach[2] (1847), who had observed with polarized light a cross in various tissues,

1. Brewster, D.: Experiments on the De-Polarization of Light as Exhibited by Various Mineral, Animal, and Vegetable Bodies with a Reference of the Phenomena to the General Principles of Polarization, Phil. Tr. Roy. Soc., London, 1815, pt. 1, pp. 21-53.

2. von Erlach, C.: Mikroskopische Beobachtungen über organische Elementarteile bei polarisiertem Licht, Arch. f. Anat. u. Physiol., 1847, p. 313.

such as nuclei of onion plant and amyloid crystals from potatoes. He stated the belief that the basis for this cross lay in the concentric arrangement of the constituent elements and pointed to the fact that the lens also showed a cross when examined between Nicol prisms. But whereas von Erlach had been interested in the lenticular cross only incidentally, Valentin [3] (1858) made a special study of it. Valentin found that the cross was a universal phenomenon in all animal lenses but most striking in those of fishes and reptiles. Dehydrating the lens with alcohol enhanced its appearance. Valentin,[4] in a second communication (1861), pointed out that a spherocrystal in which the elements are arranged radially to the optic axis is similar to the animal lens in producing the cross.

Koeppe [5] (1918-1921) described at length certain phenomena seen with polarized light but made no mention of the cross in any of the reports that were available to me. The lenticular cross was described by Schmidt [6] (1924) in his monograph on the examination of animal tissue by means of polarized light. Lenhard [7] (1933) discussed at length the optics of the phenomenon and concluded that the production of a cross by the mammalian lens showed that the birefringent micelles were arranged at right angles to the lens fibers. Lenhard was particularly interested, however, in chicken lenses, which he studied with Nicol prisms and an interference plate ("gips"). As he was unable to demonstrate birefringence in the lens of the chicken embryo before the sixth day of incubation, he concluded that the phenomenon depended in part on pressure exerted by the lens capsule.

As is evident from the foregoing references, the appearance of a cross with polarized light in various substances is not infrequent. The one characteristic all the substances that produce it have in common

3. Valentin, G.: Neue Untersuchungen über die Polarisations-Erscheinungen der Krystall-linsen des Menschen und der Thiere, Arch. f. Ophth. (pt. 1) **4**:227, 1858.

4. Valentin, G.: Aenderung des Charakters der Doppelbrechung in Krystall-linsen, Arch. f. Ophth. (pt. 1) **8**:88, 1861.

5. Koeppe, L.: (*a*) Das biophysikalisch-histologische Verhalten der lebenden Augengewebe unter normalen und pathologischen Bedingungen im polarisierten Lichte der Gullstrandschen Nernstspaltlampe, Arch. f. Ophth. **98**:171, 1919; (*b*) **102**:4, 1920; (*c*) Die stereomikroskopische Sichtbarmachung des lebenden interfaszikulären Kittliniensystems der Hornhautlamellen, sowie das Verhalten der lebenden Hornhautnerven im polarisierten Lichte der Gullstrandschen Nernstspaltlampe, München. med. Wchnschr. **67**:39, 1920; (*d*) Die ultra- und polarisationsmikroskopische Erforschung des lebenden Auges und ihre Ergebnisse, Leipzig, Ernst Bircher, 1921; abstracted, Zentralbl. f. d. ges. Ophth. **5**:519, 1921.

6. Schmidt, W.: Die Bausteine des Tierkörpers im polarisierten Licht, Monograph, Bonn, Friedrich Cohen, 1924.

7. Lenhard, O.: Ueber die Doppelbrechung der Linse, Arch. f. Augenh. **108**:1, 1934.

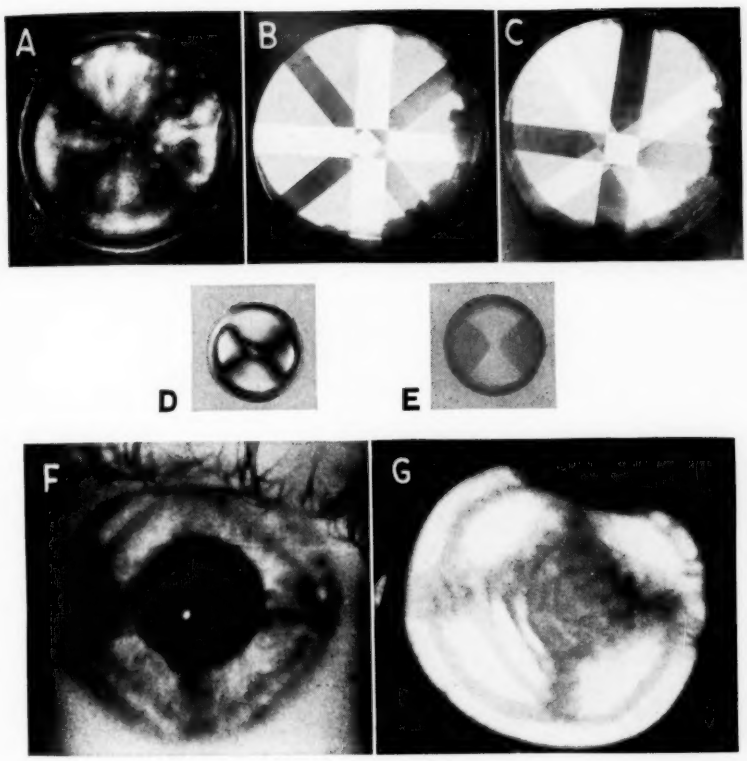
is a concentric or radial arrangement of the particles. This arrangement may be an anatomic characteristic arising from the laying down of successive layers during growth, or it may be induced by forces applied so as to cause concentric compression. Thus, a sphere of glass which is isotropic may be made to exhibit the cross if it is at first heated and then rapidly cooled by being immersed in water. The cross will disappear on reheating.

The fact that the lens of the developing chicken eye does not exhibit the phenomenon until that stage in its development in which pressure from the capsule may be effective suggests that pressure may be responsible for the concentric arrangement of the micelles. But the fact that once the phenomenon is exhibitable in the lens the capsule may be removed and the lens considerably damaged without abolition of the cross shows that the arrangement of the lens fibers is not dependent on continued pressure.

The physical explanation of the phenomenon is not entirely clear, and at present I need not enter into the controversy regarding it. The current hypotheses are presented in the articles previously referred to. I should like, however, to point out that a similar phenomenon may be produced by strips of cellophane. If eight strips of cellophane are arranged like the petals of a flower on a glass plate and examined between polaroids, a black cross may be produced by the strips which correspond to the axes of the polaroids, while the strips in the intermediary position will be light. The polaroids may then be rotated so the other four strips are dark and those formerly showing the cross will now be light (figure, *B* and *C*). One might say that in the case of cellophane—and by analogy in the case of the lens too—the production of a cross depends on a radial symmetry of the elements.

So far as I know, there is no way of seeing the cross entoptically. There is, however, a well known subjective phenomenon, known as Haidinger's brushes, which may be related to the subject and may therefore be discussed at this time.

Haidinger's brushes are difficult to describe but with patience may be consistently elicited by looking through a polaroid at a homogeneous light background, especially if the background is predominantly blue, as in the case of the sky. The brushes consist of two yellow sheaves radiating in opposite directions from the point of fixation to about 5 degrees eccentrically. The brushes occupy slightly less than quadrants, and the sectors between them stand out as intensified blue against the background. If one has difficulty in perceiving the brushes, I find that they may be brought out by a blue filter placed before the eye, in addition to the polaroid. Then dark brushes instead of yellow will be seen, separated by sectors which are brighter than the background. These are made especially conspicuous if the polaroid is rotated back and forth.



A, cross produced by the lens. *B* and *C*, phenomenon produced by strips of cellophane. *D*, human lens examined with interference plate between polaroids. *E*, drawing of Haidinger's brushes (von Helmholtz [11]). *F*, cross produced by the anterior segment of the intact eye. *G*, the phenomenon in the excised rabbit's cornea.

Rotating the polaroid causes the brushes to rotate to an equal degree and ordinarily in the same direction. A curious fact which I have observed, and to which I shall refer later, is that the insertion of a piece of cellophane between the eye and the polaroid will cause the brushes to rotate in a direction opposite to that of the polaroid. I have no explanation for this reversal of rotation.

The structure responsible for these brushes is apparently the eye, for I have been unable to form an image of them with the optical bench. Further proof that the phenomenon is ocular in origin and not environmental is the fact that when seen through a telescope the brushes remain the same absolute size despite changes in the size of images of the environmental objects.

The brushes were first described by Haidinger in a series of articles (1844-1854).[8] It is not evident, however, that he had any clearcut idea as to their origin. In one of his final papers [8h] on the subject he suggested that the phenomenon depends on the chromatic aberration of the eye. The lens was suggested as a source of the phenomenon by von Erlach [2] (1847), Brewster [9] (1850), Schrötter [10] (1856) and Valentin [3] (1858), but most of the subsequent reports have ascribed the phenomenon to the radial fibers of the macula. Von Helmholtz [11] expressed this view perhaps most comprehensively and pointed to the fact that the appearance of the brushes is consistent with their being an entoptic projection of Henle's fiber layer. He stated that the phenomenon was not due to multiple refraction at the boundaries of the ocular media, as had been previously suggested, on the grounds that such a hypothesis was inconsistent with the following facts: the phenomenon is seen only with light containing blue; the brushes do not increase in distinctness toward the periphery, and the center of the phenomenon is at the point

8. Haidinger, W.: (*a*) Ueber das direkte Erkennen des polarisierten Lichts, Ann. d. Phys. u. Chem. **63**:29, 1844; (*b*) Ueber komplimentäre Farbeneindrücke bei Beobachtung der Lichtpolarisationsbüschel, ibid. **67**:435, 1846; (*c*) Beobachtung der Lichtpolarisationsbüschel in geradlinig polarisiertem Licht, ibid. **68**:73, 1846; (*d*) Beobachtung der Lichtpolarisationsbüschel auf Flächen, welche das Licht in zwei senkrecht aufeinander sehenden Richtungen polarisierten, ibid. **68**:305, 1846; (*e*) Das Interferenzschachbrettmuster und die Farbe der Polarisationsbüschel, ibid. **85**:350, 1850; (*f*) Dauer des Eindrucks der Polarisationsbüschel auf der Netzhaut, ibid. **93**:318, 1854; (*g*) Beitrag zur Erklärung der Farben der Polarisationsbüschel durch Beugung, ibid. **91**:291, 1854; (*h*) Einige neuere Ansichten über die Natur der Polarisationsbüschel, ibid. **96**:314, 1854.

9. Brewster, D.: On the Polarizing Structure of the Eye, in Report of the 20th Meeting of the British Association for the Advancement of Science, Cambridge, England, Cambridge University Press, 1850, pt. 2, p. 5.

10. Schrötter, A.: Personal communication to Haidinger; cited by Haidinger.[8h]

11. von Helmholtz, H.: Helmholtz's Treatise on Physiological Optics, translated by J. P. C. Southall, Ithaca, N. Y., The Optical Society of America, 1924, vol. 2, pp. 304-308.

of fixation and not on the optic axis. Since von Helmholtz' analysis there has been general acceptance of the view that the retina is the sole tissue responsible for the phenomenon, and the possibility that the lens may play a part is not even considered in modern textbooks.[12]

I was led, however, to suspect that the lens may play a role in the production of Haidinger's brushes because of the similarity of the brushes to the following phenomenon produced by the lens in vitro: If one places an animal or human lens between crossed polaroids and then inserts an interference plate, such as cellophane or mica, between the lens and either polaroid, one may produce the appearance of yellow brushes on a blue background. These brushes are strikingly similar to those seen subjectively. When the cellophane is inserted, it apparently rotates the plane of polarization, and the cellophane must be rotated empirically to a point at which the brushes are found best. They then are quite like those seen subjectively. If my analogy is correct, one must assume that in the eye there is, thus, not only an analyzer but an interference plate. The anatomic basis for this is not known to me. *E* in the illustration is a picture representing the subjective phenomenon, while *D* is a picture taken of a human lens in vitro under the conditions already described. There is one basic difference between the entoptic and the in vitro phenomenon, and that is the persistence of the brushes during rotation of the polaroid in the former case and their disappearance in the latter. This difference may be due to the difference in the arrangement of the interference plate in the 2 cases. With the in vitro

12. Duke-Elder (Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1, p. 806) stated: "Haidinger's brushes are probably due to the double refracting action of the parallel arrangement of the radial fibers of Henle around the fovea."

Viallefont (in Bailliart, P.; Coutela, C.; Redslob, E., and Velter, E: Traité d'ophtalmologie, Paris, Masson & Cie, 1939, vol. 2, p. 455) stated: "cette image (Haidinger's brushes) serait en rapport, d'aprés la majorité des auteurs, avec la double réfraction des rayons lumineux et l'arrangement parallele des fibres de Henle autour de la fovéa" ("this image [Haidinger's brushes] would be in agreement, according to the majority of authors, with the double refraction of luminous rays and the parallel arrangement of the fibers of Henle around the fovea").

Ebbecke (in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1929, vol. 12, pt. 1, p. 260) wrote: ". . . auf der besonderen Anordnung der nervösen und bindegewebigen Radiärfasern die nicht wie sonst senkrecht zur Limitans externa sondern mehr parallel dazu radiär zur Mitte verlaufen, beruht die Erscheinung der Haidingerschen Polarisationsbüschel—und einen der entoptischen Macula entsprechenden Raum einnehmen" (". . . on the special arrangement of the nervous and connective tissue radial fibers, which do not as others run vertically to the limitans externa, but more parallel to it about the center, depends the phenonemon of Haidinger's polarization brushes—and corresponds in space to the entoptic macula").

phenomenon, however, there is some rotation of the brushes with that of the polaroid before their disappearance, and like the subjective phenomenon, the insertion of an additional piece of cellophane causes a reverse rotation of the brushes.

This experimental production in the lens of a phenomenon which has such striking similarity to Haidinger's brushes suggests that the lens may be responsible for the phenomenon. I have found, however, that an excised cornea so suspended in water that its shape is preserved as well as possible will also show the brushes under the same conditions as did the lens. I suspect, therefore, that the phenomenon is dependent on the radial arrangement of the tissue, and it is altogether possible that a macula would likewise manifest it. I was unable to obtain a retina with a macula for examination. But that the phenomenon is not exclusively characteristic of the macula is suggested by the preceding data. It also is apparent from these data that the yellow color of the brushes does not depend on the yellow pigment of the macula, as was assumed by von Helmholtz.[11]

CROSS PRODUCED BY THE ANTERIOR SEGMENT OF THE INTACT EYE

If one illuminates the intact eye by polarized light and examines it through an analyzer, the plane of which is set at right angles to that of the polarizer, one sees a black cross apparently on the iris (figure, *F*). Although this phenomenon may be readily seen with any ophthalmoscope equipped with polaroids, it has not to my knowledge been noted heretofore in the literature, and hence I will first describe it briefly.

The phenomenon consists of a dark cross on an illuminated iris. The arms of the cross are approximately 2 mm. wide and extend to the limbus. Centrally their point of intersection is usually lost in the red reflex from the pupil. The cross is therefore the more clearcut the smaller the pupil. The tips of the cross are connected by several alternately dark and light (usually colored) bands giving a diamond shape to the figure. When the analyzer and polarizer are rotated together, as when the ophthalmoscope in which they are set is turned, the cross will rotate to an equal extent and in the same direction. If, however, either polaroid is rotated independently, the cross will show slight rotation but disappear after the polaroid has been rotated more than a few degrees. The cross does not reappear on continued rotation of the polaroid until the polaroid has been turned approximately 180 degrees from its original position. Thus, in this respect, at least, it is similar to the lenticular cross.

The phenomenon is elicited equally with eyes in vivo and after enucleation.

One's first impression is that the phenomenon comes from the iris, as the cross is made up of bands in which the iris is not visible. That the iris is not alone responsible for the phenomenon is, however, proved by examining the iris of an eye from which the cornea has been removed. The cross is then not present. And, furthermore, the cross is present when the iris is made invisible by injecting milk or, better still, ink into the anterior chamber.

The phenomenon is thus evidently due to the cornea, and two possibilities present themselves: first, that the phenomenon is one of reflection from the corneal surface and, second, that it is one of transmission through the cornea. The first possibility can be quickly disposed of, for the phenomenon is not present with prostheses, in which the reflection is similar to that of the eye, and it is present and essentially unchanged even when the corneal surface is distorted, as in bullous keratitis, or when the refractive and reflecting power of the cornea is reduced almost to zero by the application of a flat contact glass. I am therefore led to conclude that the phenomenon is determined by transmission through the cornea and is thus analogous to that previously described for the lens. The essential difference between the two phenomena is that while one appears on examination of the lens between crossed polaroids, the other appears on examination of the cornea between a polaroid on the one side and a surface, presumably the iris, which reflects the polarized light on the other side. That the reflecting surface does not depolarize the light is proved by the very presence of the phenomenon. This maintenance of polarization I would not have predicted, as the iris examined in the absence of the cornea shows complete depolarization. I have no satisfactory explanation for this apparent inconsistency, although it is possible that the exposed iris affects the polarization in a manner different from that of the iris of the intact eye.

Although there are several reports in the literature on examination of the cornea with polarized light (Brewster,[1] 1815; von Ebner,[13] 1882; Valentin,[8] 1858; Nordenson,[14] 1921, and Koeppe,[5] 1918-1921), I am aware of only three references to a corneal cross. One paper was by His[15] (1856), who noted that a black cross was visible if the cornea of small animals (frogs) was removed and examined between crossed Nicol prisms. A second article was by von Fleischl[16] (1880), who

13. von Ebner, V., quoted by Nordenson.[14]

14. Nordenson, J.: Ueber die Grösse der Doppelbrechung der Hornhautsubstanz, Arch. f. Ophth. **105**:721, 1921.

15. His, W.: Beiträge zur normalen und pathologischen Histologie der Cornea, Basel, Schweighauser, 1856.

16. Fleischl, E.: Ueber eine optische Eigenschaft der Cornea, Sitzungsb. d. k. Akad. d. Wissensch. Math.-Naturw. Cl. **82** (pt. 3):47, 1880.

similarly examined excised corneas between Nicol prisms. Von Fleischl stated that the cross was visible only with stretching of the cornea and interpreted this as showing that the cornea under normal conditions was isotropic. A third reference to the cross was made by Schiötz [17] (1882), who observed that when the cornea was bound on to the end of a glass tube and examined between Nicol prisms, a cross could be seen.

The chief difference between these observations and those of mine previously noted is that my observations were made on the intact eye. His found the cross on small but not on large corneas, owing, I presume, to the fact that the larger corneas when excised do not keep their shape sufficiently well under ordinary conditions. Thus, I was unable to observe the cross in the excised rabbit's cornea until I had allowed the cornea to swell in physiologic solution of sodium chloride overnight. The cornea then assumed and maintained a shape similar to that before it was excised, and the cross, as well as the colored rings at the periphery, became visible (figure *G*). I cannot agree with von Fleischl's conclusions. I presume we both observed the same phenomenon, that of a cross produced by polarized light transmitted through the cornea. But contrary to what von Fleischl reported, I observed that the cross is present with the normal cornea. Whereas von Fleischl stated the belief that the cross is present only with increased intraocular pressure, I found it present and unchanged when the intraocular pressure was reduced to zero by paracentesis, and I observed, furthermore, that raising the intraocular pressure by squeezing the enucleated eye between one's fingers does not enhance the cross. It is evident, therefore, that despite von Fleischl's conclusions, the production of the cross does not require increased intraocular pressure.

The optical principles involved in the production of a corneal cross are dealt with by von Fleischl. The explanation for the corneal cross is undoubtedly similar to that for the lenticular cross. Both cornea and lens produce the phenomenon by means of the symmetric arrangement of their constituent elements. Polarized light transmitted through the cornea or lens will therefore show the same alterations as when transmitted through any uniaxial crystal.[18] According to Wood,[19] all the rays (of plane-polarized light) striking a crystal plate at an axis parallel to or at right angles to the polarizer will be completely stopped by a Nicol prism held behind the plate at a proper degree of rotation (thereby producing the cross).

---

17. Schiötz, H.: On Certain Optical Properties of the Cornea, Nord. med. ark. **14** (no. 28):1, 1882.

18. The isochromatic rings produced by uniaxial crystals with monochromatic light have also been reported in the crystalline lens.[3]

19. Wood, R. W.: Physical Optics, New York, The Macmillan Company, 1929, pp. 321-322.

SUMMARY

Two ocular phenomena produced with polaroids are described.

The first is exhibited by the lens and consists of a dark cross on a light background. Such a phenomenon is seen with other structures, in which, owing to growth or pressure, the elements are arranged radially or concentrically.

A model to illustrate the phenomenon can be made with radially arranged cellophane strips.

Although Haidinger's brushes are generally assumed, in the absence of experimental confirmation, to be due to the macula, a strikingly similar phenomenon can be produced by the lens and cornea in vitro.

The second ocular phenomenon is exhibited by the anterior segment of the intact eye. This, like that from the lens, consists of a dark cross seen against a light background. The second phenomenon is due to the cornea and like the lenticular cross depends on a radial or concentric arrangement of the elements. It is produced by the normal cornea and does not depend on increased intraocular pressure.

THE EYE AND SLEEP

JAMES E. LEBENSOHN, M.D., PH.D.
CHICAGO

Fifty years ago, on May 30, 1890, a Viennese ophthalmologist, Ludwig Mauthner, announced in an informal communication before the Vienna Medical Society an original conception of the mechanism of sleep.[1] The disease now known as epidemic lethargic encephalitis was then radiating from northern Italy to the adjacent Austrian provinces. Mauthner remarked that all chronic forms of sleeping sickness in common have as a complication ptosis and ocular muscle paralysis and macroscopically show engorgement of the walls of the third ventricle and the sylvian aqueduct. Hence he conceived that physiologic sleep depends on a temporary suspension of function of the periventricular gray matter which thus interrupts conduction both to and from the cortex. The drooping of the lids in drowsiness and the simultaneous diplopia, according to his theory, indicate that the innervational disturbance of sleep extends to the adjacent oculomotor nuclei. Mauthner's notion of a sleep regulation center was ignored for a quarter of a century. As late as 1914, Dejerine, holding the chair of neurology at Paris hallowed by Raymond and Charcot, asserted with finality, "Sleep cannot be localized." But in 1916, Economo, after exhaustive study of the morbid anatomy of lethargic encephalitis and also of other forms of epidemic encephalitis, revived the idea, which has since been convincingly demonstrated both pathologically and experimentally. Commenting on scientific progress, Fosdick, president of the Rockefeller Foundation, aptly said: "Only rarely does one man or one group of men recite with clear, loud tones a whole important chapter, or even a whole important paragraph, in the epic of science. Much more often the start comes from some isolated and perhaps timid voice, making an inspired suggestion, raising a stimulating question. This first whisper echoes about the world of science, the reverberation from each laboratory purifying and strengthening the message, until presently the voice of science is decisive and authoritative."

Read before the Chicago Ophthalmological Society, May 13, 1940.

From the Department of Ophthalmology, Northwestern University Medical School.

1. Mauthner, L.: Proceedings of the Viennese Medical Society, Wien. klin. Wchnschr. **3**:445, 1890.

LUDWIG MAUTHNER

Ludwig Mauthner was born in Prague a century ago, April 13, 1840. At 16 he matriculated at the University of Vienna and at 18 presented before the Vienna Academy of Sciences his first contribution, "The Structure of the Spinal Cord of the Lower Vertebrates." At 21 he received his medical degree and, choosing ophthalmology as his specialty, came under the stimulating influence of von Graefe, Donders and Bow-

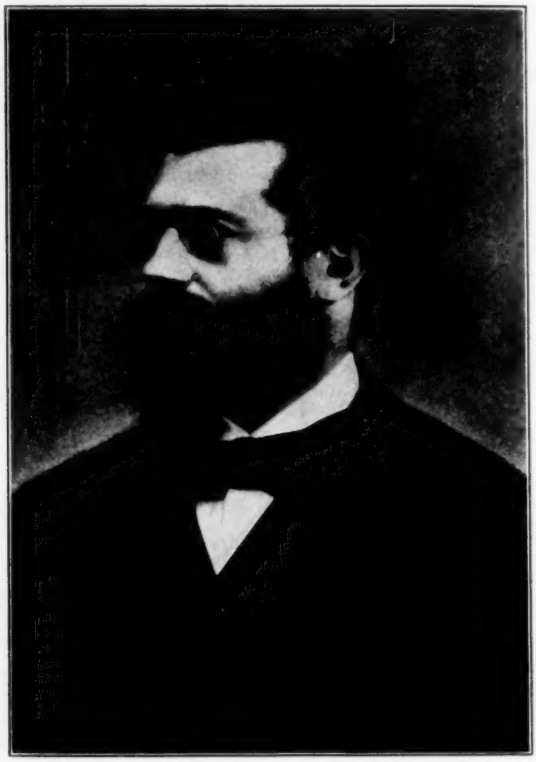


Fig. 1.—Ludwig Mauthner, Viennese ophthalmologist, discoverer of the sleep regulation center.

man. Back in Vienna, his clinical chief was fortunately the discerning Eduard von Jaeger. A fervid friendship developed, based on reciprocal admiration. Jaeger gave him a free hand, saying "Ich bin es der Augenheilkunde schuldig, Mauthner die vollste Freiheit auf meiner Klinik zu gewähren- denn er ist ein Genie." ("I owe it to ophthalmology to give Mauthner a free hand in my clinic—for he is a genius.") In 1868, at the age of 28, he contributed the first comprehensive text on ophthalmoscopy, with 468 plates and a full bibliography. The school of medi-

cine was opened at Innsbruck in the following year, and Mauthner was called to the chair of ophthalmology. But the new school was not popular, and the town offered little in clinical material or private practice. During his incumbency Mauthner published an exhaustive work on the optical errors of the eye and edited the German edition of Knapp's *Archives of Ophthalmology and Otology.* After eight years (in 1877) the advent of mental disturbance in his wife prompted his resignation from this irksome post and a return to Vienna. This act antagonized the members of the Ministry of Education, who for years thereafter excluded Mauthner from any appointment under their control.

In Vienna Mauthner achieved fame as a lecturer and published a series of monographs covering almost every field of ophthalmology. In 1890 he became associated with the Policlinic, and in 1894 he was selected to follow the succession of von Jaeger and Stellwag von Carion in the chair of ophthalmology at the University of Vienna. Concerning Mauthner's demise, Hirschberg wrote dramatically: "Reality is more tragic than all tragedies. For seventeen years Mauthner had with unwavering efforts striven for the one place which he considered the highest good—the position of Professor Ordinarius in the Medical Faculty of Vienna. On October 19, his nomination for this place is made public; On the following night he dies, 54 years of age—like the leader of an army after the victorious battle." [2] On March 19, 1899, his friend Schnabel spoke at the unveiling of a memorial bust of marble placed in the arcade of the Vienna University. Karl Lindner informed me last summer that Mauthner was of Jewish birth and that this monument is still there.

THE SLEEP PROCESS

Excitation of the hypothalamus produces wakefulness; the destruction thereof, sleep (Ranson [3]). The hypothalamus lies at the base of the brain, in the lower part of the third ventricle, above the hypophysis and below the thalamus, and extends from just behind the optic chiasma backward to the opening of the cerebral aqueduct. Physiologically the term includes the tuber cinereum, the corpora mamillaria and the adjacent nuclear masses. The region immediately in front of the hypothalamus probably constitutes a parasympathetic center from which fibers descend to the posterior lobe of the pituitary and to the nuclei of the parasympathetic cranial nerves. The posterior lobe of the pituitary may bear a relation to the parasympathetic nervous system similar to that of the thyroid and adrenals to the sympathetic nervous system. The hypothalamic center governs the activities of the sympathetic nervous system

2. Hirschberg, J.: Ludwig Mauthner, obituary, Am. J. Ophth. **11**:386, 1894.

3. Ranson, S. W.: Somnolence Caused by Hypothalamic Lesions in the Monkey, Arch. Neurol. & Psychiat. **41**:1 (Jan.) 1939.

and is the region also concerned with sleep rhythm, metabolism and body temperature. The emotional drive exerted by the hypothalamus, modified by cortical control, maintains the waking state. Drowsiness is combated by drugs that increase cortical or sympathetic activity—caffeine, amphetamine, ephedrine and thyroid. Descartes was not so wrong when he assigned to the soul a central position in the brain, for according to Penfield [4] and Spiegel [5] the indispensable substratum of consciousness probably lies in the interbrain.

Kleitman [6] concluded with Mauthner that sleep is due to a functional break between the cortex and the lower centers, the positive Babinski sign in sleep being thus explainable. A marked decrease of afferent impulses effectively reduces the excitability of the hypothalamic center. Closing the eyes and relaxing the limbs remove most of the stimuli that maintain wakefulness. The diurnal periodicity of sleep is determined by the diurnal variations of muscle tonus, metabolic rate, body temperature and cortical activity.

OCULAR CONCOMITANTS OF SLEEP

The several periods of sleep per day in infancy are consolidated to one unbroken rest during the night as human reactions become more dependent on visual than on tactile and olfactory stimuli.

Diurnal Performance.—Loss of sleep in the adult interferes with the learning process but otherwise does not apparently affect mental or physical power unless continued to great length. The temperature is lower, performance worse and fatigability greater immediately on arising than just before retiring. The highest body temperature, the best performance rate (including visual reaction time) and the lowest fatigability are all reached in the afternoon.[6] Bogoslovsky [7] found that the sensitivity of the dark-adapted eye to the electric current rose from 9 a. m. to 12:30 p. m. and then fell irregularly to a minimum at midnight.

In a personal study of the power of the upper lid, weights were attached by serrefine forceps to the lashes of both upper lids near their internal and external ends (fig. 2). With the frontalis muscle restricted by an elastic bandage, the palpebral fissure can open to a width of 11 mm. With 10 Gm. of weight on each upper lid the fissure can maintain a width of 7 to 10 mm. for seventy to ninety seconds; with 20 Gm. the

4. Penfield, W.: The Cerebral Cortex and Consciousness, in Harvey Lectures, 1936-1937, Baltimore, Williams & Wilkins Company, 1938.

5. Spiegel, E. A.: Bemerkungen zur Theorie des Bewustseins und zum Schlafproblem, Ztchr. f. d. ges. exper. Med. **55**:183, 1927.

6. Kleitman, N.: Sleep and Wakefulness, Chicago, University of Chicago Press, 1939.

7. Bogoslovsky, A. I.: Diurnal Changes in the Electrical Sensitivity of the Eye, Bull. biol. et méd. expér. URSS **3**:127, 1937.

lid stays open 3 to 3.5 mm. for fifteen to twenty-five seconds. With 40 to 50 Gm. weights the upper lid cannot be lifted above the margin of the lower lid. With 20 Gm. weights on each upper lid the opening and closing movements can keep time with a metronome set at 100 beats per minute for twelve to twenty minutes. The tests showed considerable individual differences but from 10 a. m. to 10 p. m. failed to disclose a significant diurnal variation.

Vigil.—While a person is awake there is little rest from visual activity; hence it is not surprising that in prolonged vigil the chief

Fig. 2.—Studying the power of the upper lid. Serrefine forceps are attached to the lashes of the upper lid. Each pair weighs 10 Gm.

complaints are ocular. Pain in the eyes associated with itching, burning, dryness and grittiness becomes more troublesome on each successive night and is tremendously exaggerated by any attempt to read. The eyelids droop without closing and are kept open with difficulty. If they are closed, a positive Romberg sign develops from the general muscular tonelessness. The cornea loses its brightness, and edema of the lids and dark circles under the eyes become evident. The pupillary response remains brisk, though the pupillary area, measured in dim lights of standard intensity, is reduced to three fourths of its initial value by the

third night.[8] Convergence fails; by the fourth day it is impossible to fixate the printed page,[9] and a manifest exotropia of 4 to 5 prism diopters can be measured.[10] Whereas the eyes in the alert state can rotate horizontally through a 40 degree angle in one-tenth second, in extreme drowiness it takes twice as long and the fixation is unsteady.[11] After an eighty hour vigil all the abnormal ocular findings, both subjective and objective, have disappeared after the third night of rest.[10]

Physiologic Sleep.—Sleep begins with a spastic closure of the lids by the orbicularis muscle. As the levator muscle becomes toneless a flaccid closure follows, muscular twitchings cease and the folds in the lid smooth out. The lid closure of sleep is an inherited association, occurring in the newborn and in the congenitally blind. It is always complete unless prevented by an abnormal condition, such as shortness of the lids or weakness of the orbicularis muscle. The sleep of the blind does not differ in quantity or quality from that of the seeing.[12] With the closing of the lids the eyeballs assume their position of rest (Bell's phenomenon), which in 90 per cent of adults is above the horizontal level, most frequently up and out. A shift in the sleeping position of the eye with development indicates that this resting status is a consequence of binocular vision. The eyes are up in only 0.9 per cent of newborn infants, in 20 per cent of blind children and in 42 per cent of children 1 year old.[13] Ocular movements are observable in sleep which probably originate from reflex disturbance. In children pendular oscillations decrease with the depth of sleep from 10 to 1 per minute.[14] In an adult in deep sleep slow disjunctive movements may be seen,[15] reminiscent of the ocular performance in the first few weeks of life.

---

8. Lee, M. A., and Kleitman, N.: Attempts to Demonstrate Functional Changes in the Nervous System During Experimental Insomnia, Am. J. Physiol. **67**:141, 1923.

9. Katz, S. E., and Landis, C.: Psychologic and Physiologic Phenomena During a Prolonged Vigil, Arch. Neurol. & Psychiat. **34**:307 (Aug.) 1935.

10. Herz, F.: Selbstbeobachtung über freiwillige Schlafentziehung, Arch. f. d. ges. Physiol. **200**:429, 1923.

11. Miles, W. R.: Horizontal Eye Movements at the Onset of Sleep, Psychol. Rev. **36**:122, 1929.

12. Kreidl, A., and Herz, F.: Der Schlaf des Menschen bei Fernbleiben von Gesichts-und-Gehörseindrucken, Arch. f. d. ges. Physiol. **203**:459, 1924.

13. Hall, A. J.: Some Observations on the Acts of Closing and Opening the Eyes, Brit. J. Ophth. **20**:257, 1936.

14. DeToni, G.: I movimenti pendolari dei bulbi oculari dei bambini durante il sonne, Pediatria **41**:489, 1933.

15. Pietrusky, F.: Das Verhalten der Auge im Schlafe, Klin. Monatsbl. f. Augenh. **68**:355, 1922.

The conjunctiva is congested in sleep, and the cornea is often dull owing to overlying mucous shreds, desquamated epithelium and conjunctival secretion, the brightness returning after a few movements of the lid are made.[15]

Closing the eyes in the waking state is followed by marked dilatation of the pupils, and the electroencephalogram from the occipital cortex gives the typical alpha rhythm of rest. In sleep, however, the pupil is constricted, the degree of constriction increasing with the depth of sleep, and the encephalogram changes to that indicative of decreasing cerebral activity. In infants less than 3 months old the pupil never attains the marked constriction found in adults in deep sleep. Both the direct and the consensual light reaction can be definitely elicited in sleep, as well as pupillary dilatation to sensory and acoustic stimulation, but the deeper the sleep the slower and less the response.[15]

With the opening of the lids on awakening the pupils instantly dilate, even though the sleeper is aroused by illumination. As the eyeballs revert to the position of parallelism and fixation an evanescent horizontal diplopia can be demonstrated, which, because of its fleeting nature, is seldom perceived. Rozner [16] has shown that this occurs even when the bulb occupies the midposition in sleep. In a darkened room he placed a red glass before one eye of a sleeper and held a lighted candle in front. Immediately on being aroused, the subject experienced an exophoria of 2 to 3 prism diopters.

Pathologic Sleep.—The ocular findings in pathologic sleep have been most thoroughly studied in lethargic encephalitis. In this disease the oculomotor nuclei nearest the hypothalamus are frequently involved. Three ocular phenomena dominate the acute stage of the disease—ptosis, diplopia and obscuration of vision, connoting nuclear lesions of the nerves governing the external muscles of the eye and accommodation. Mydriasis is more common than miosis, and the pupils fail to react in accommodation more often than to light. Invasion of Perlia's nucleus affects convergence, producing paresis or spasm, the so-called paralysis of divergence being probably the latter effect. Oculogyric crises signify a release in control of that portion of the pallidum devoted to movements of the head and eyes.[17] Just closing the lids precipitated sleep in some of Stockert's encephalitic patients.[18] Provided their eyes were open the patients could keep completely awake even in the total darkness.

16. Rozner, E.: Schlafzentrum und seine Beziehungen zur Diplopie bei Schlaftrunkenheit, Med. Klin. **31**:205, 1935.

17. Shapiro, S. L.: Otologic Findings in Oculogyric Crises, Arch. Neurol. & Psychiat. **34**:714 (Oct.) 1935.

18. von Stockert, F. G.: Die Beziehungen der Augenmuskeln zum Schlaf, Med. Klin. **29**:697, 1933.

INTERPRETATION

All the ocular concomitants of sleep can be explained as a sequence of muscular fatigue and depression of sympathetic and cortical activity, these three effects being interrelated. There are no afferent sympathetic fibers. The sympathetic hypothalamic center is dependent on somatic stimuli for excitation, among the most important of which is muscle tone. Excitation of the hypothalamus is the indispensable substratum of cortical activity. During the waking state the oculomotor musculature is constantly active, and relaxation from the strain can be obtained only by sleep. The cerebral importance of the muscles of the head and neck is indicated by an area of localization much larger than that of all the other muscles combined.

With depression of the sympathetic nervous system the deep layer of the levator muscle is thrown out of action; the upper eyelid droops, and the loss of power stimulates the antagonistic orbicularis muscle to activity. Lacrimation ceases; the eyes are dry; "the sandman comes." Loss of vasomotor tone accounts for conjunctival congestion, dark circles below the eyes and edema of the lids. Vascular dilatation renders the papillary elevations of the palpebral conjunctiva prominent. Vasodilatation is the cause of photophobia;[19] excites production of mucus and conjunctival secretion with the accompanying sensations of grittiness, veiled vision and haloes, and by its trophic disturbance precipitates the desquamation of corneal and conjunctival epithelium to which the complaint of burning is related. With inadequate sleep the epithelial repair remains uncompleted and the burning sensation may continue for a while the next morning. As the day advances and the sympathetic center regains its vigor the eyes feel better, till night falls, drowsiness comes and the cycle returns.

For the extreme miosis of deep sleep cerebral inactivity is more responsible than sympathetic depression. Like the positive Babinski sign present in sleep, it represents an absence of inhibitory cortical control over the lower motor centers.

DEDUCTIONS CONCERNING CONJUNCTIVAL ASTHENOPIA

The syndrome called chronic catarrhal conjunctivitis presents a clinical picture of ocular reactions almost identical with those following lack of sleep. That the similarity is striking is revealed by a representative description of the former condition, such as this by McKee:[20]

"The subjective symptoms are characteristic. The patients complain of great eye discomfort, which is usually worse at night and after the

19. Lebensohn, J. E.: The Nature of Photophobia, Arch. Ophth. **12**:380 (Sept.) 1934.

20. McKee, S. H., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 386.

use of the eyes, especially for near work. The heaviness of the eyelids becomes so marked that the patient has difficulty in keeping the eyes open. Complaint is made of something in the eye and of an itching and burning feeling . . . the papillae of the conjunctiva become swollen and turgid, giving the membrane a rough and granular appearance. In this form, there is a moderate swelling and congestion of the conjunctiva and but slight secretion, the symptoms being more those of hyperemia."

Since the condition just described is not a true conjunctivitis, some prefer the term "hyperemia of the conjunctiva." A clinically more useful designation is "conjunctival asthenopia," since the symptoms must often be differentiated from those of accommodative, muscular and aniseikonic asthenopia.

A number of patients with this condition give on questioning a history of inadequate sleep due to insomnia or to the necessities of work or parenthood. Adjustment of the sleep habits and a zinc collyrium will bring prompt recovery. For those whose sleep is disturbed by light the use of the comfortable sleep shade now commercially available should solve the difficulty.

In another significant proportion of cases the condition is stubborn and often familial, and the patients go from oculist to oculist, changing their glasses frequently. The symptoms tend to continue with remissions and recurrences through the lifetime of the patient. The frequent resistance to local and hygienic treatment favors the impression that an obscure systemic disturbance is the basis for the trouble. The cause has been sought, with occasional success, in allergy, endocrine dysfunction, vasomotor imbalance and vitamin deficiency. The resemblance of the syndrome to the ocular symptoms of loss of sleep gave me the suggestion that in many cases the underlying cause is a depression of activity of the sympathetic nervous system for which the logical treatment would be the administration of a sympatheticomimetic drug.

The most serviceable remedy proved to be desiccated thyroid, which is effective, well tolerated, simple to administer, easy to control, stable and cheap. This stimulant was reserved for cases in which the condition was intractable and those in which there were other symptoms suggestive of impaired sympathetic function, such as slow pulse, low body temperature, listlessness, tiredness, allergic susceptibility and meteorologic sensitiveness. The contraindications are tachycardia and arterial hypertension. A satisfactory response is generally secured with single small doses, of ½ to 1 grain (0.03 to 0.06 Gm.), daily. In the cases investigated the basal metabolic rates ranged from +1 to −21 per cent, but a report on basal metabolism is only occasionally required; the pulse rate is the guide to management. The danger signs, loss of weight and a pulse rate over 100, rarely occur with this dosage. The thyroid either stimulates the production of epinephrine or sensitizes the mecha-

nisms on which epinephrine acts. The effect of thyroid medication is slow to develop but long sustained. After a single intravenous injection of thyroxin forty-eight hours may elapse before any effect is detectable, but the activity may persist after a fortnight.

The results of therapy have been most encouraging. Of several hundred cases observed in the past few years a few representative records will be briefly cited.

REPORT OF CASES

CASE 1.—A salesman aged 24 was 5 feet 9 inches (175 cm.) tall and weighed 148 pounds (67 Kg.). He found reading difficult and complained of headaches, dyspepsia and restlessness. He slept eight hours or more and awakened with his eyes and body as tired as before. The pulse rate was 66, and the temperature was 97.4 F. Cycloplegic refraction gave the following results: right eye +0.25 D. cyl., axis 90, vision 20/15; left eye, —25 D. sph., vision 20/15. The basal metabolic rate was —16 per cent. Thyroid, ½ grain (0.03 Gm.), was administered daily, with relief of all symptoms.

CASE 2.—A housewife aged 40 complained that her eyes were always tired and that she had vague pains in her nose and ears. There had been recurrent headaches for the past fifteen years. She was 5 feet 6 inches (168 cm.) tall and weighed 150 pounds (68 Kg.). The pulse rate was 64 and the temperature 98.2 F. She wore the needed correction: right eye, +4.00 D. sph. ⊃ +0.25 D. cyl., axis 90, vision 20/20; left eye, —3.75 D. sph. ⊃ +0.50 D. cyl., axis 90, vision 20/20. Further examination disclosed right hyperphoria of 2 prism diopters. One prism diopter was incorporated in her lens, without much benefit. The basal metabolic rate was —21 per cent. Thyroid, 1 grain (0.06 Gm.) daily, gave complete relief.

CASE 3.—An accountant aged 30 complained that he was tired and unable to use his eyes for near work. He had been treated by a prominent ophthalmologist, who prescribed weak plus cylinders and an astringent collyrium, but he felt no better. Thyroid, ½ grain (0.03 Gm.) daily, was prescribed, and recovery ensued. No change was made in the glasses or in the local medication. Five years later he returned with a mild recurrence. Thyroid was again prescribed, with the same satisfactory response.

CASE 4.—A dentist aged 38 had been troubled with his eyes since youth. He brought with him four pairs of glasses from four different physicians: First pair, +0.25 D. cyl., axis 90, in each lens; second pair, the same prescription, tinted, with 1 prism diopter base out in each lens; third pair, a similar prescription with 1 prism diopter base down for the right eye, and the fourth pair, special reading glasses with +0.50 D. sph. added to the prescription. Cycloplegic examination indicated: right eye, emmetropia; left eye, +0.25 D. sph. ⊃ +0.25 D. cyl., axis 85. There was normal vision in each eye. The near point was 17 cm. No glasses were advised. A 0.2 per cent zinc sulfate collyrium was ordered, and thyroid, ½ grain (0.03 Gm.) daily, was prescribed. For the past three years he has been working comfortably.

CASE 5.—A baker aged 28 came under my care for syphilitic involvement of the third nerve. He was 5 feet 11 inches (180 cm.) tall and weighed 200 pounds (9 Kg.). In the course of his visits he complained of burning of his eyes. Zinc sulfate solution and cold compresses were prescribed, without benefit. He

was advised in addition to instill epinephrine hydrochloride (1:1,000), but still he obtained no relief. He would awaken from sleep with his eyes burning; then they would lacrimate and burn even more. Thyroid, 1 grain (0.06 Gm.) daily, was ordered, and the following week his eyes were comfortable.

CASE 6.—An office worker aged 23 complained of headaches and difficulty in reading. Otherwise he felt normal except that he was somewhat nervous, ate much and could not gain weight. He was 6 feet 2 inches (188 cm.) tall and weighed 135 pounds (61.2 Kg.). He had had four pairs of glasses in the past three years. Cycloplegic examination gave the following results: right eye, + 0.50 D. cyl., axis 5, vision 20/15; left eye, + 0.50 D. cyl., axis 105, vision 20/15—, which was essentially the same as that worn. There was esophoria of 7 prism diopters at 20 feet (6 meters). Orthophoria was present at 14 inches (35 cm.). He has now been taking ½ grain (0.03 Gm.) of thyroid daily for eighteen months. The pulse rate is 75. His headaches and nervousness are gone; his eyes are comfortable, and he is unconscious of his muscular trouble. He has gained 40 pounds (18 Kg.), but for the past three months his weight has been constant. When he was last reexamined, a week prior to the time of writing, he had become, curiously, 1 D. more myopic, the cycloplegic correction being: right eye, — 0.50 D. sph. ⌒ — 0.25 D. cyl., axis 88, with vision 20/15; left eye, — 0.75 D. sph. ⌒ — 0.25 D. cyl., axis 15, with vision 20/15. The esophoria for distance remained as before.

SUMMARY

To an ophthalmologist, Ludwig Mauthner, belongs the credit of discovering the now recognized sleep regulation center. The excitability of the hypothalamus and consequent wakefulness are maintained by peripheral stimulation. A great reduction of impulses is followed progressively by lowering of sympathetic tone, depression of cortical activity and sleep. The ocular apparatus in drowsiness evidences impaired sympathetic function by drooping lids, dry eyes and congested conjunctiva. A similar syndrome in certain cases of intractable conjunctival asthenopia, sometimes called chronic catarrhal conjunctivitis, suggests that the underlying cause is likewise an impairment of sympathetic function. In such cases the basal metabolic rate is generally somewhat below normal. The condition is relieved by administration of a small dose of thyroid daily.

58 East Washington Street.

DRUSEN OF THE OPTIC PAPILLA

A CLINICAL AND PATHOLOGIC STUDY

BERNARD SAMUELS, M.D.
NEW YORK

According to its scientific programs, only once in its long history has the attention of the American Ophthalmological Society been called to drusen (hyaline bodies) of the optic papilla. This was in a paper read by de Schweinitz in 1891, the first American contribution on drusen of the papilla. It was based on a single case, and it was unique in that the author reported the result of not only the clinical but also the postmortem examination. The concretions were confined to the papilla and were found nowhere else, although a careful search was made of the optic nerves in their entire lengths and of the brain. Strange to say, since 1921, except for a brief paper published by Goldstein and Givner in 1933, this subject has received but scant notice in the literature.

Clinically and pathologically drusen of the papilla are rare. They are still rarer in the retina. In neither location are they to be confounded with drusen of the choroid, which are familiar to all.

In this paper I venture to give a résumé of a microscopic study of preparations from 20 globes in which drusen of the papillae were found, in the belief that an endeavor to correlate the anatomic and clinical features of these uncommon drusen will serve to revive an interest in them and to bring out information of practical use.

LOCATION

All of the drusen studied, with the exception of those in 1 case (fig. 1, *2*), were located anterior to the lamina cribrosa. In the exceptional case a single hyaline druse lay just posterior to the lamina cribrosa in the trunk of the optic nerve. A similar finding has apparently been reported but once before, in a case described by Sachsalber in 1901, in which drusen were encountered both anterior and posterior to the cribrosa. In the present case the druse lay in contact with the central connective tissue strand of blood vessels and was surrounded by a delicate mantle of endothelial-like cells. It was found in a globe with a normal fundus which had been enucleated on account of an epithelioma of the cornea.

Read at the Seventy-Sixth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 5, 1940.

The druse was believed to be a corpus arenaceum, although far removed from the common location in the intervaginal space. It was surmised that in the process of invagination of the pial sheath to form the central connective tissue strand of the optic nerve a small cord of arachnoidal tissue was invaginated. In this way endothelial cells had produced a misplaced corpus arenaceum.

An especially frequent place of localization was on the nasal side in the recess between the overhanging scleral spur and the lamina cribrosa. Occasionally scattered drusen were found in the papilla anterior to the level of the choroid. These superficial drusen were usually present when large drusen occupied the deep sclerochoroidal canal. The impression was sometimes given that drusen may start in the recess under the scleral spur and later come forward by way of the narrow canal. The sections were all horizontal. Several times hyaline nodules were encountered on either side of the central blood vessels. They may have formed a ring embracing the blood vessels, just as a sheet of bone sometimes surrounds the papilla.

NUMBER, SIZE AND STRUCTURE

There were usually a number of drusen. In a majority of the cases they were of considerable size. Frequently a large druse was surrounded by many small ones having a sandlike aspect. The outlines were usually irregular and jagged, not smooth as the ophthalmoscopic appearance may suggest. Their consistency was generally such that they seemed to cause no more resistance to the microtome than other structures. In only 4 globes did the drusen show true calcification. A few suggested a laminated structure.

REASONS FOR ENUCLEATION

Practically all the globes had been severely damaged; otherwise they would not have come to enucleation. In 7 cases there had been secondary glaucoma. In 2 other cases the papilla appeared to be otherwise normal. Apparently, in secondary glaucoma leading to gliosis of the retina and in pigmentary degeneration of the retina the papilla is particularly prone to produce drusen. The relation between drusen and gliosis and pigmentary degeneration of the retina is frequently mentioned in the literature. Striking were 4 cases in which deep undermined excavations were filled with newly formed neuroglia tissue, in the midst of which drusen were deposited.

AGE OF THE PATIENTS

Age seemed to play little part in the formation of the drusen. The ages of the patients when known ranged, with a single exception, from 10 to 42 years. The important predisposing factor was considered to

be some local disease of long duration within the globe itself. In 1 instance, in which a globe had been removed shortly after an injury, it was certain that the drusen in the papilla had long antedated the injury as a separate condition.

EPIPAPILLARY DRUSEN

As a rule, drusen occurred in the middle and deeper layers of the papilla and did not approach the vitreous surface. However, 1 preparation was of special interest because drusen were found not within the papilla but actually on its surface, embedded in a glial membrane (fig. 1, *18*). This preparation was figured by A. Fuchs in his "Atlas of the Histopathology of the Eye." Evidently these particular concretions were the product of a metaplastic process in new-formed neuroglia tissue. In this case the original irritation that caused the production of the glial membrane probably dated back over a period of years to a perforating ulcer of the cornea. Later a staphyloma developed, which was excised. In this way there could have been produced a reaction in the glial membrane itself resulting in the formation of drusen. I reported a case of an analogous epiretinal druse in 1939 in a paper on drusen of the retina, in which was described a mass of drusen that lay in a glial membrane on the surface of the retina.

ORIGIN OF DRUSEN OF THE PAPILLA

Lauber, in 1921, in a paper on the clinical and pathologic aspects of drusen of the optic papilla, stated the opinion that papillary drusen are invariably the product of cells from the pigment epithelium that have migrated into the sclerochoroidal canal. As a matter of fact, pigmented epithelial cells are never seen in the papilla, as are "clump cells" in the iris. It is unbelievable that a druse could be formed either by a deposition of material derived from pigmented epithelial cells or by a transformation of these cells without leaving traces of pigment to reveal the process.

The formation of hyaline bodies in various structures of the globe is not infrequent. Drusen of the choroid are acknowledged to be the product of the pigment epithelium by a process of deposition, as is often suggested by their laminated structure. Verhoeff has more than once pointed to an analogy between drusen of the lamina vitrea and hyaline concretions sometimes encountered in the thickened corneal epithelium of globes with keratitis bullosa. Hyaline bodies in old corneal scars are well known. When irritated, the epithelium on the posterior surface of the anterior lens capsule produces a peculiar hyalinized tissue, the anterior polar cataract. It would not be strange, therefore, if the glial cells of the papilla under the influence of irritation should take on abnormal activity and secrete hyalin. The theory was advanced by

A. Fuchs in his atlas. The frequent association of drusen of the papilla with secondary glaucoma and retinitis pigmentosa, each characterized by a proliferation of glial cells in the papilla and retina, speaks in favor of this hypothesis. Evidence that glial cells may produce hyalin is afforded

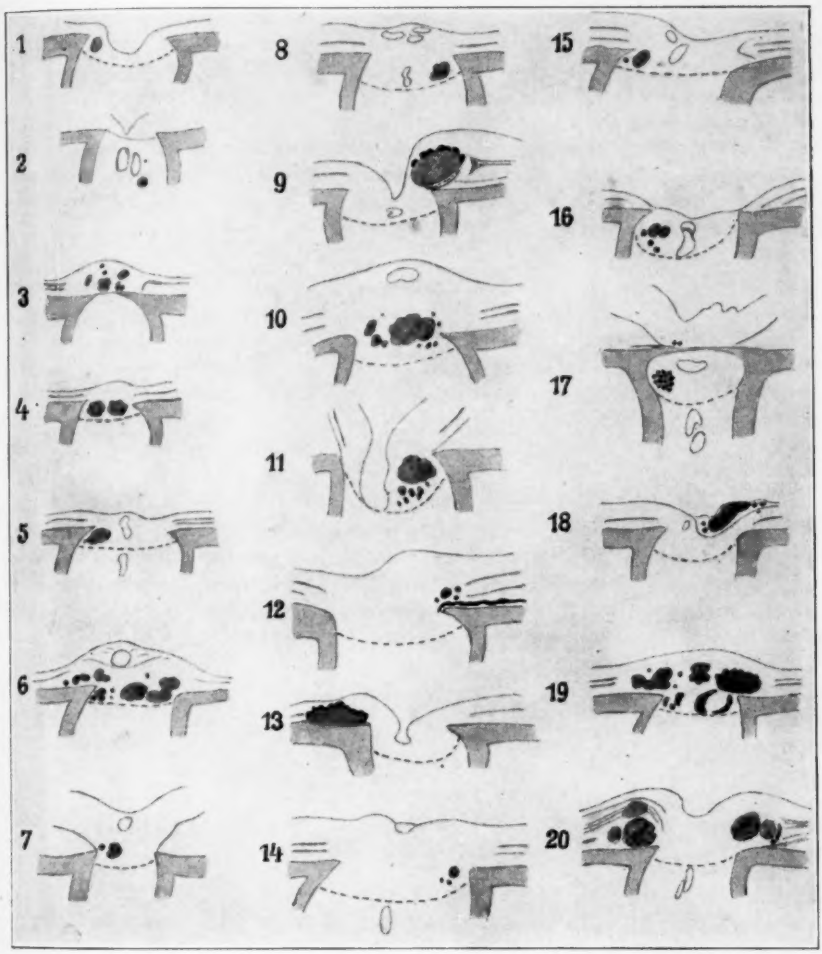


Fig. 1.—A sketch of a preparation derived from each case of drusen studied. The oval rings signify blood vessels.

by the instances in which drusen were found in pure glial tissue on the surfaces of the retina and papilla. It is likely that every druse starts with a deposit of minute globules of hyaline which fuse and then increase in size by successive accessions. Separate drusen may coalesce to form larger ones, which for this reason have uneven surfaces.

PIGMENTED CIRCUMPAPILLARY DRUSEN

The collection included 3 examples of drusen which in point of origin belonged to the lamina vitrea but in point of location belonged to the papilla. They were spoken of as "transitional drusen."

CASE 1.—A boy aged 14 had become blind ten years previously, after an injury to the eye. The cornea was staphylomatous and had undergone hyaline degeneration. One large round hyaline druse was found at the nerve and stood out because of the following features (fig. 1, *9*): First, it jutted into the substance of the papilla from the margin of the choroid; second, it lay under a covering of pigmented epithelial cells, and third, a sliver of bone formed the choroidal side of the druse. Clearly, the pigment epithelium of the choroid had proliferated into the papilla, producing a misplaced concretion. Within the druse an interesting process took place, namely, a direct transformation of hyalin into bone and this without calcification.

CASE 2.—A boy 14 years of age had an eye which became blind from spontaneous iridocyclitis. Adjoining the rim of the papilla (fig. 1, *13*) an elongated druse sprang from the lamina vitrea and protruded into the retina and papilla. Its free surface was jagged. The formation lay under a heavily pigmented covering. It overhung a deep pathologic excavation filled with a mass of glial cells. This was an additional example of a druse in association with an extensive proliferation of glial cells. It is evident that this druse belonged primarily to the lamina vitrea but had grown out of bounds.

CASE 3.—A man 26 years of age had had for four years an inflammation of the globe, which followed perforation by a foreign body, with steadily failing vision. Of interest were a number of large roundish concretions projecting into the marginal tissue of the papilla (figs. 1, *20* and *2 B*). Their texture and the manner in which the pigment was distributed along their surfaces gave them the appearance of an adenoma of the ciliary body and permitted the assumption that they were the product of the pigment epithelium. It was astonishing that drusen were found nowhere else on the lamina vitrea. Possibly edema of the papilla followed the perforation of the ulcer which stimulated the pigment epithelium to produce concretions.

The "transitional drusen" were all hyaline. In no instance was there a primary druse within the papilla.

NONPIGMENTED CIRCUMPAPILLARY DRUSEN

Specimens showed small roundish nonpigmented drusen in the peripheral tissue of the papilla (fig. 1, *12* and *19*). There was no link between them and the pigment epithelium; neither could drusen be found in the outlying retina. The presence of drusen elsewhere in the papilla pointed to a papillary origin.

In this connection emphasis is laid on the fact that the papilla may be invaded by drusen of the retina. Jaeger and I each reported clinically such a case. Accompanying circumpapillary drusen it is not uncommon to see minute glistening satellites in the neighboring healthy fundus.

CIRCUMPAPILLARY THICKENING OF THE LAMINA VITREA

During the study examples of uniform thickening of the lamina vitrea at the margin of the papilla were encountered. At its papillary rim the pigment epithelium is normally heavier than elsewhere, often

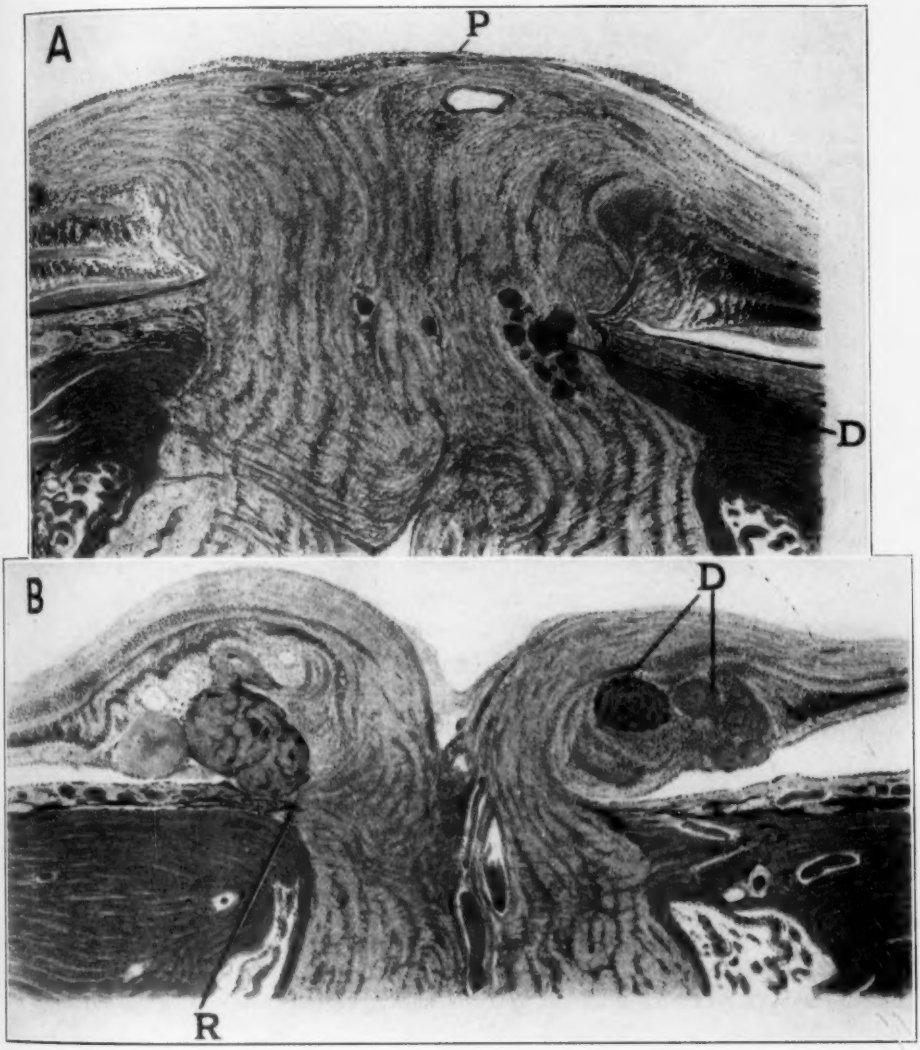


Fig. 2.—*A*, drusen (D) in the sclerochoroidal canal. The nerve head is swollen. *P* points to an epipapillary membrane. The drusen are mostly on the nasal side (see fig. 1, *10*). *B*, circumpapillary drusen (*D*) derived from the pigment epithelium of the choroid. The retina (*R*) shows relative retraction of nerve fibers (see fig. 1, *20*).

revealing itself as the so-called choroidal ring. It is understandable that in pathologic preparations this zone, richer in pigment than others, commonly shows a uniform thickening of the lamina vitrea and, if the irritation has been severe enough, drusen.

PRACTICAL POINTS

1. *Distribution.*—According to the specimens (fig. 1, *1, 5, 6, 8, 10, 11, 12, 15, 16, 17* and *19*) the nasal side of the nerve head seems to be

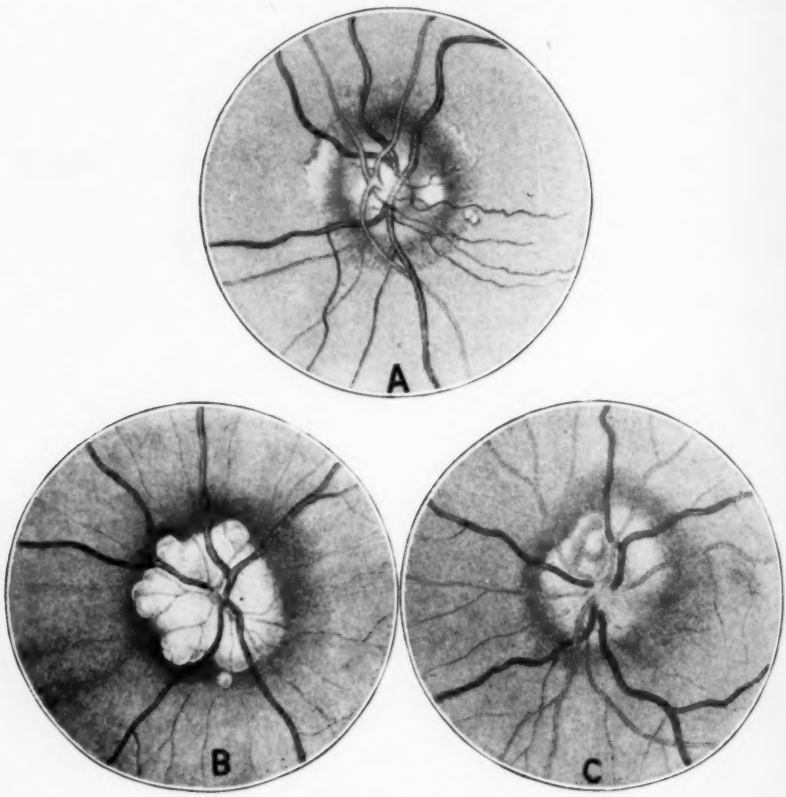


Fig. 3.—*A*, an eye of a man aged 30, showing circumpapillary drusen derived from the papilla. Other drusen are in the center, and a number of satellites are present. *B*, an eye of a woman aged 30, showing an otherwise normal fundus and a coating of drusen which seals off the nerve head and elevates the blood vessels, simulating papilledema. Below is a druse of the retina. *C*, deep drusen in an otherwise healthy eye. The picture simulates optic neuritis. The drusen above approach the surface.

the site of predilection for drusen, just as it is for glial membranes. It is here that they are apt to attain their largest size. The papilla is thicker on the nasal side, and consequently there is more glial tissue to produce drusen.

2. *Depth.*—A. Drusen deep within the sclerochoroidal canal, unless they are large, are probably invisible with the ophthalmoscope because of a thick covering of nerve fibers and capillaries. Deep drusen give an abnormal fulness and density to the ophthalmoscopic picture of the papilla, which may be accompanied by an enlargement of the blindspot. In many cases so-called pseudoneuritis probably owes its appearance to deeply seated, unsuspected drusen. If one nerve head appears to be normal and the other shows pseudoneuritis or "slight optic neuritis," one should be suspicious of drusen in the latter. In the history of more than 1 patient there was mention of pseudoneuritis in the fellow eye. The papillae are usually affected in unequal degree.

B. Drusen anterior to the choroidal ring, being nearer the surface but never breaking through it, may reflect the light with such luster and brilliancy as almost to baffle description. They have been described as causing the nerve head to protrude 4 mm. into the vitreous. They may extend into the surrounding retina and cause, in addition to an increase in elevation, an enormous increase in diameter, after the manner of papilledema (fig. 1, *6* and *19*).

Regarding the retinal blood vessels, the drusen may be anterior or posterior to them. Occasionally the blood vessels are completely hidden for a stretch in a mass of drusen. Probably the most remarkable case on record was the one reported by Noyes in 1895 in which the papilla and the surrounding retina, for a distance of about half the normal disk diameter were buried under a mass of hyaline nodules, the summit of which stood 9 D. above the outlying fundus.

3. *Presence or Absence of Pigment.*—Drusen in the center of the papilla never show pigment. There is no doubt that they are true primary drusen. Drusen at the periphery may encompass the papilla with a narrow, notched and gleaming border; this is the zone of "transitional drusen." The absence of pigment here indicates origin in the papilla or retina; its presence indicates origin in the pigment epithelium. In the substance along the border there may conceivably be an intermingling of drusen of the papilla, of the retina and of the pigment epithelium. The border of the papilla is also a favorite site for formation of bone.

4. *Age.*—Clinically a druse of large size would be considered an old one. Under the microscope the age is judged not only by size but by content. The presence of calcium would point to long duration. It is doubtful whether a calcified druse can be distinguished with the ophthalmoscope from a noncalcified one. A minute islet of druse is certainly not likely to contain chalk, and yet it may sparkle like a diamond.

RELATION BETWEEN DRUSEN AND VISION

It has always been a subject of comment how well preserved the vision may be, even when the papilla is packed to overflowing with drusen. There are anatomic grounds for the retention of vision and for comparison between a papilla distended by clear fluid, as in papilledema, and one distended by drusen.

The structure of the papilla anterior to the level of the choroidal ring lends itself readily to distention. The nerve bundles as they emerge from the lamina cribrosa lose every vestige of the connective tissue system that completely separates them in the lamina cribrosa. Neither is there present in the papilla the system of supporting fibers which knits the various stratums of the retina together and prevents separation and consequently any great amount of swelling. On the other hand, in the papilla the sole support retained by the bundles and fibers is the delicate glial tissue. For this reason the nerve fibers of the papilla may be widely displaced without being ruptured and still be able to perform their function. Indeed, there may be an element of edema in every papilla that contains many drusen. In several specimens the nerve fibers at a distance from the concretions were definitely separated by fluid, as in papilledema. Such a condition would explain the swollen edematous aspect lent by some nerve heads to the ophthalmoscopic picture.

In an analysis of the effect of the presence of drusen on vision, doubtless location is an important factor. Drusen in the narrow unyielding sclerochoroidal canal would be more likely to cause pressure atrophy of the nerve fibers, accompanied by changes in the field, than those in the more loosely expanded tissues anteriorly. It may well be that an old calcified inert druse with a jagged border acquires with the years a toxic and irritating effect on the nerve fibers that it did not possess as a new-formed pure hyaline body.

GROWTH AND PROGNOSIS

Iwanoff, in 1868, in a paper on optic neuritis, described concretions anterior to the lamina cribrosa in 6 cases. Liebreich in his remarks on this paper stated that he was the first to behold these bodies ophthalmoscopically. This was ten years after Müller had discovered them pathologically and predicted that some day they would be seen clinically. From that time to this clinicians have remarked on the property of drusen of the papilla as a rule to remain for years without any visible change in size and aspect. With drusen of the choroid it is different, for they may be seen to develop and to increase in size and numbers in a relatively short time. It is true, papillary drusen have been observed to grow. In a great many of the cases of drusen of the papilla reported

the patients have been young, healthy persons, even as young as 8 years, whose eyes were otherwise normal. There is probably a constitutional basis for such early spontaneous growths. Drusen of the papilla have come to be associated with youth and drusen of the choroid with senescence.

The prognosis of drusen of the papilla is considered to be good. In the literature the vision is as often as not recorded as normal, even when there is a tremendous mass of drusen. It is doubtful that drusen alone have ever caused total blindness; nearly always there has been mentioned some fortuitous and contributing disease.

BIBLIOGRAPHY

Müller, H.: Arch. f. Ophth. (pt. 2) **4**:1, 1858.

Iwanoff: Klin. Monatsbl. f. Augenh. **6**:421, 1868.

Nieden, A.: Centralbl. f. prakt. Augenh. **2**:6, 1878.

Jany: Centralbl. f. prakt. Augenh. **3**:167, 1879.

Oeller, J. N.: Arch. f. Augenh. **8**:435, 1879.

Lawson, G.: Tr. Ophth. Soc. U. Kingdom **3**:117, 1883.

Stood, W.: Klin. Monatsbl. f. Augenh. **21**:506, 1883.

Story, J. B.: Tr. Ophth. Soc. U. Kingdom **3**:102, 1883.

Hirschberg, J.: Centralbl. f. prakt. Augenh. **8**:46, 1884.

Masselon, J.: Mémoires d'ophthalmoscopie. Infiltration vitreuse de la rétine et de la papille, Paris, O. Doin, 1884.

Schäfer, H.: Centralbl. f. prakt. Augenh. **8**:203, 1884.

Ancke, R.: Centralbl. f. prakt. Augenh. **9**:167, 1885.

Hirschberg, J., and Birnbacher, A.: Centralbl. f. prakt. Augenh. **9**:65, 1885.

Remak: Centralbl. f. prakt. Augenh. **9**:257, 1885.

Nettleship, E.: Tr. Ophth. Soc. U. Kingdom **6**:358, 1886.

Wedl, C., and Bock, E.: Pathologische Anatomie des Auges, Vienna, C. Gerolds Sohn, 1886, p. 299.

Gessner, C.: Arch. f. Augenh. **18**:297, 1888.

Rath, W.: Arch. f. Ophth. (pt. 4) **34**:81, 1888.

Nieden, A.: Arch. f. Augenh. **20**:72, 1889; Arch. Ophth. **18**:198, 1889.

Gurwitsch, M.: Centralbl. f. prakt. Augenh. **15**:225, 1891.

Hirschberg, J., and Cirincione, G.: Centralbl. f. prakt. Augenh. **15**:166, 1891.

Purtscher, O.: Centralbl. f. prakt. Augenh. **15**:292, 1891.

de Schweinitz, G. E.: Tr. Am. Ophth. Soc. **6**:349, 1891.

Terson, A.: Arch. d'opht. **12**:367, 1892.

Peters: Allg. Ztschr. f. Psychiat. **50**:1093, 1894.

de Schweinitz, G. E.: Tr. Am. Ophth. Soc. **7**:212, 1894.

Jaeger, E.: Ophthalmoskopischer Hand-Atlas, edited by M. Salzmann, Leipzig, F. Deuticke, 1894.

Gifford, H.: Arch. Ophth. **24**:395, 1895.

Heyl, A. G.: Tr. Am. Ophth. Soc. **7**:355, 1895.

Streiff, J. J.: Mikroskopische Untersuchungen über Altersveränderungen der Vasa centralia retinae, nebst einem Beitrag zur Kenntnis der Concremente des Opticus und seiner Scheiden und einer kurzen Betrachtung über die von Fuchs beschriebene periphere Sehnervenatrophie, Thesis, Zürich, 1898, Utrecht, 1898.

Thomson, E. G.: Post-Graduate **13**:954, 1898.

Mendel, F.: Centralbl. f. prakt. Augenh. **24**:242, 1900.

Nieden, A.: Ztschr. f. Augenh. **3**:361, 1900.
Sachsalber, A.: Beitr. z. Augenh. **5**:865, 1901.
Morton, A. S., and Parsons, J. H.: Tr. Ophth. Soc. U. Kingdom **23**:135, 1903.
Baas, K.: Arch. f. Ophth. **57**:571, 1904.
Cirincione, G.: Clin. ocul. **5**:1599, 1904.
Demaria, B.: Klin. Monatsbl. f. Augenh. **42** (pt. 1):339, 1904.
Hanke: Ztschr. f. Augenh. **11**:86, 1904.
Streiff, J. J.: Klin. Monatsbl. f. Augenh. **42** (pt. 1):149, 1904.
Rabitsch, F.: Klin. Monatsbl. f. Augenh. **43** (pt. 1):72, 1905.
Bonhoff, J. K.: Bericht über die Wirksamkeit der Universitäts-Augenklinik zu Giessen, vom. 1. April 1903 bis zum 31. März, 1904, Thesis, Giessen, O. Kindt, 1906.
Harman, N. B.: Tr. Ophth. Soc. U. Kingdom **26**:318, 1906.
Schuster, P.: Arch. f. Augenh. **54**:364, 1906.
Elschnig, A., and Lauber, H.: Arch. f. Ophth. **65**:428, 1907; p. 435 and plate 19, fig. 5.
Lauber, H.: Ztschr. f. Augenh. **17**:391, 1907.
Höeg, N.: Arch. f. Ophth. **69**:355, 1908.
Lauber, H.: Arch. f. Ophth. **68**:1, 1908.
Topolanski, W.: Ztschr. f. Augenh. **20**:584, 1908.
Chevallereau: Rec. d'opht. **31**:103, 1909.
Fejér, J.: Arch. f. Ophth. **72**:454, 1909.
Kärnbach: Monatschr. f. prakt. Tierh. **21**:481, 1910.
Silva, R.: Klin. Monatsbl. f. Augenh. **49** (pt. 2):379, 1911.
Wetzel, E.: Ueber Drusenbildung im Sehnervenkopfe und in der Retina, Thesis, Rostock, 1911.
Coats, G.: Tr. Ophth. Soc. U. Kingdom **32**:119, 1912.
Paderstein: Centralbl. f. prakt. Augenh. **36**:18, 1912.
Wilbrand, H., and Saenger, A.: Die Neurologie des Auges, Wiesbaden, J. F. Bergmann, 1912, vol. 4, pt. 2, p. 495.
Köhler, H.: Zur Kasuistik der Drusen im Sehnervenkopf, Thesis, Giessen, O. Kindt, 1913.
Lauber, H.: Ztschr. f. Augenh. **29**:201, 1913.
Juler, F. A.: Tr. Ophth. Soc. U. Kingdom **34**:177, 1914.
Waardenburg, P. J.: Nederl. tijdschr. v. geneesk. **2**:690, 1917; abstracted, Klin. Monatsbl. f. Augenh. **59**:690, 1917.
Viner, G.: Brit. J. Ophth. **2**:426, 1918.
Stargardt: Deutsche med. Wchnschr. **45**:1374, 1919.
Fuchs, E.: Arch. f. Ophth. **103**:304, 1920.
Lauber, H.: Arch. f. Ophth. **105**:567, 1921.
Tobler, T.: Ztschr. f. Augenh. **47**:215, 1922.
Goldstein, I., and Givner, I.: Calcified Hyaline Deposits (Drusen) in Optic Disk, Associated with Pigmentary Changes in Retina, Arch. Ophth. **10**:76 (July) 1933.
Samuels, B.: Tr. Ophth. Soc. U. Kingdom **59**:715, 1939.

DISCUSSION

DR. F. H. VERHOEFF, Boston: I should like to ask Dr. Samuels whether he has ever seen drusen ophthalmoscopically and then had the opportunity to see them microscopically, or whether his conclusions were drawn, as they usually are, by seeing the drusen microscopically

and then imagining what they would look like ophthalmologically. I suppose some one has had the opportunity to see them ophthalmoscopically and then to examine them microscopically. Pigmented drusen of the disk are produced by pigmented epithelium, just as the so-called drusen of the choroid are. Dr. Samuels did not mention it, but such drusen can become organized. I remember one specimen in which a large druse just in front of the lamina cribrosa had been converted entirely into bone. I have never been able to make up my mind as to the exact origin of the very translucent nonpigmented drusen.

DR. ALLEN GREENWOOD, Boston: I want to mention a patient I saw sixteen years ago, sent to me in consultation by the late Dr. Maude Carvill, the first woman who had the honor of being a member of this society. This patient was presented at a meeting of the New England Ophthalmological Society. She was a young girl with drusen on the papilla, and instead of being like the pictures passed around the drusen were practically all about the same size and were all slightly yellowish. At the time I presented the patient in Boston I said that it looked as though the papilla had been covered by a shower of gold coins which had been spilled on the papilla. The whole papilla was entirely covered, and the drusen spread onto the retina some distance. I have never seen anything like it before or since, and I thought it would be wise to mention it here.

DR. BERNARD SAMUELS, New York: In answer to Dr. Verhoeff's question, so far as I know there have been only 2 cases in which drusen have been seen clinically and described pathologically. One of these was observed by de Schweinitz in 1892 and the other by Fowler (?) in about 1921. In one of these cases the patient was first seen clinically, and the clinical description corresponds to the anatomic and microscopic picture of drusen.

As to their origin, I did touch on that in my paper. I agree that they are due to the proliferation of glial cells. This is borne out by the fact that the drusen of the retina are found anterior to the retina in the glial cells. One sees this anterior to the outlines of the nerve and glial proliferation, so that the drusen are due to the action on the part of the glial cells, probably to some irritation.

SECONDARY GLAUCOMA DUE TO THE LENS

PARKER HEATH, M.D.
DETROIT

Practically all the tissues of the eye are capable in some manner of causing secondary glaucoma. Increased intraocular pressure is anticipated, with rupture of the capsule and lens matter streaming into the anterior chamber. The same is true of the lens luxated into the anterior chamber with the capsule intact. This tissue in the vitreous, it is well known, is also a cause of recurring iridocyclitis and associated glaucoma. Other mechanisms by which the lens induces glaucoma are, however, clinically less common and less well known. Even without actual conclusive proof, the lens may frequently be suspected of being the indirect or direct factor producing abnormally high intraocular pressure. Clinical records have been reviewed and material of the pathologic laboratory has been studied in the hope of constructing a classification of glaucoma attributable to abnormality of the lens. This classification is made up of two groups: 1. Glaucoma with the lens in position, suspended by the zonule. 2. Glaucoma with the lens out of position, partly suspended or luxated.

GLAUCOMA WITH THE LENS IN POSITION

1. There may be a defectively developed lens and iris with vascular strand remnants, or there may be a partly absorbed lens and a persistent vascular membrane, frequently associated with congenital strands across the filtration angle or with imperfect differentiation of the angle. In these rare circumstances the angular defect is probably the main cause of the glaucoma.

2. Contact of the lens with the ciliary processes leads to hypothetic vasomotor disturbance and edema of the ciliary processes. With the occurrence of edema and an increase in bulk, the lens is pushed forward. As the iris–ciliary body angle increases, the anterior chamber is rendered shallow, and ultimate blockage of the filtration angle follows. Acute edema of the ciliary body and processes with associated extravasations of blood and fibrin following corneal wounds may result in the develop-

From the Department of Ophthalmology, College of Medicine, Wayne University, Detroit.

Read at the Seventy-Sixth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 4, 1940.

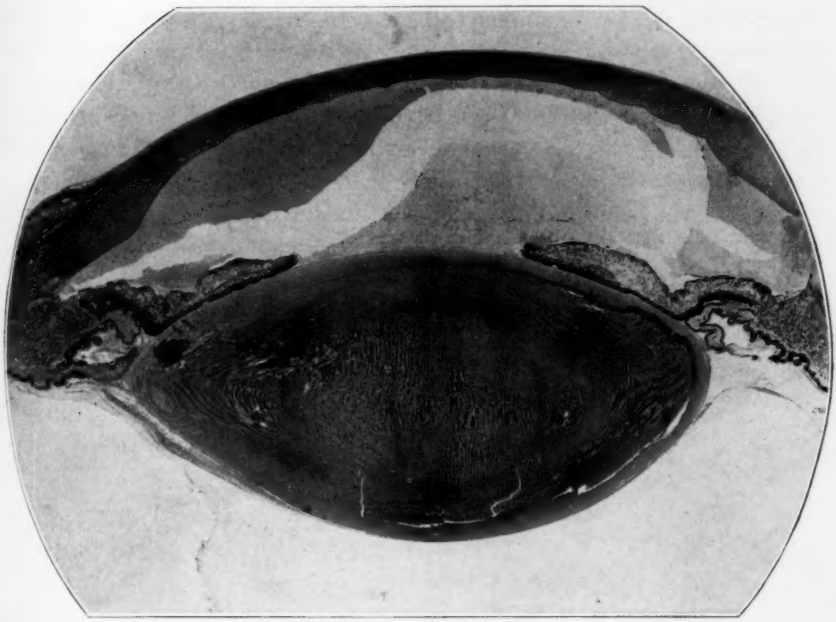


Fig. 1.—Lens out of position, in contact with the edematous ciliary processes. The condition is traumatic. The anterior chamber is deep.

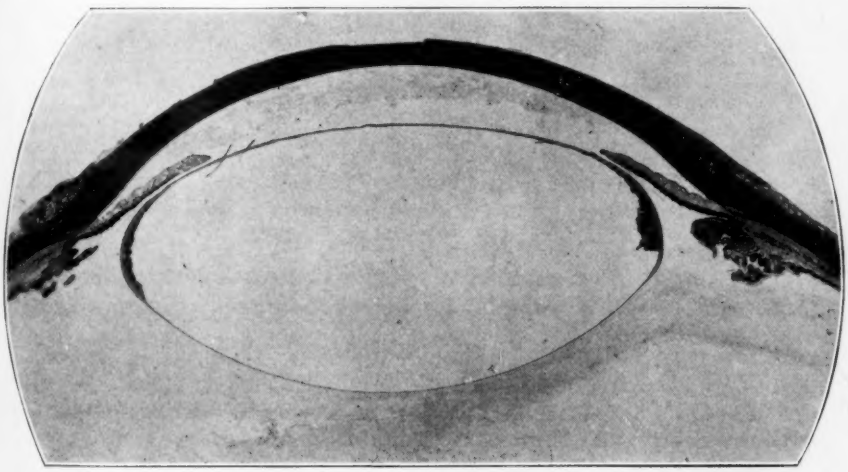


Fig. 2.—Large senile lens. The iris is pushed forward. The anterior chamber is shallow. Glaucoma is present.

ment of acute glaucoma by this route (Greeff;[1] Friedenwald[2]). As was pointed out by Scammon and Hesdorffer,[3] the growth of the lens in both weight and bulk is at a steady increase between the ages of 20 and 90 years, in proportion to the age. This increase in weight and bulk is associated with a stretching of the lens capsule. There may be, in addition, an increase of permeability of the lens capsule. Some patients show, through colobomas of the iris, the zonule partly pulled off and the zonular layer of the lens capsule detached. The ciliary processes also increase in length and width with advancing years. The intumescent lens, owing to increase of bulk, can conceivably be associated with irritative contact with ciliary processes.

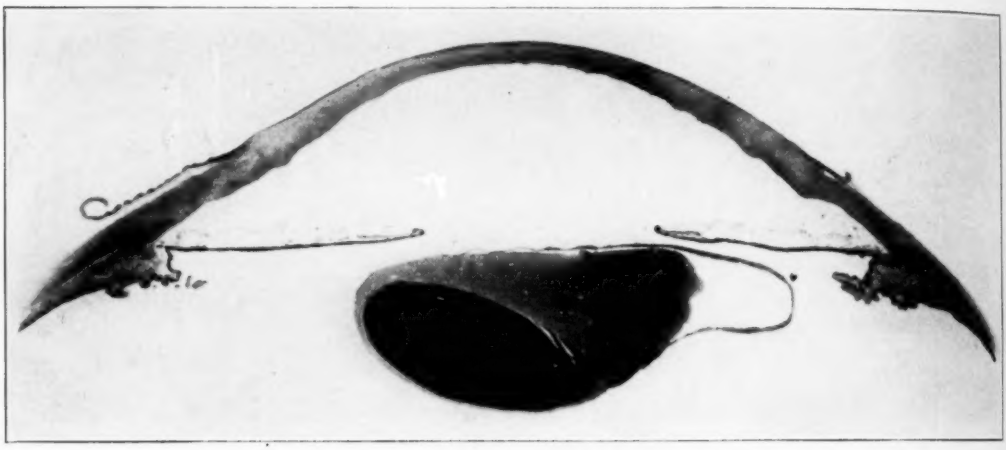


Fig. 3 (E. Fuchs).—Hypermature lens; nuclear "floats" in a toxic fluid cortex.

As was pointed out by Hess[4] and by Reese,[5] alterations in position of the ciliary processes are also found. These are due to: (1) advancing age; (2) perforation of the globe; (3) glaucoma, and (4) congenital misplacement.

3. Secondary glaucoma may occur, due to toxic substances escaping through the permeable capsule of a hypermature lens (capsule intact).

1. Greeff, R.: Pathologische Anatomie des Auges, in Orth, J.: Lehrbuch der speciellen pathologischen Anatomie, Berlin, A. Hirschwald, 1902-1906, p. 250.

2. Friedenwald, J. S.: Some Factors Concerned in the Success of Operations for Glaucoma, Am. J. Ophth. **15**:189 (March) 1932.

3. Scammon, R. E., and Hesdorffer, M. B.: Growth in Mass and Volume of the Human Lens, Arch. Ophth. **17**:104 (Jan.) 1937.

4. Hess, C.: Ueber individuelle Verschiedenherten des normalen Ciliarkörpers, Arch. f. Augenh. **67**:341, 1910.

5. Reese, A. B.: The Ciliary Processes, Am. J. Ophth. **17**:422 (May) 1937.

The same mechanism may explain those rare cases in which there is monocular glaucoma showing lens opacification of the complicated type without other evidences of uveitis. There may be an increase of permeability of the ciliary epithelium due to the toxic lens substance. Another rarely seen secondary glaucoma of this type presents a calcified lens and a dense cyclitic membrane.

4. Desquamation of the capsule may produce glaucoma by toxic, irritative and mechanical methods. Increased hyalinization and sclerosis of the sclerocorneal trabecula may be associated with flaking of the capsule. The percentage of glaucoma occurring in patients with both this disease and desquamation is high enough to be significant. Patients

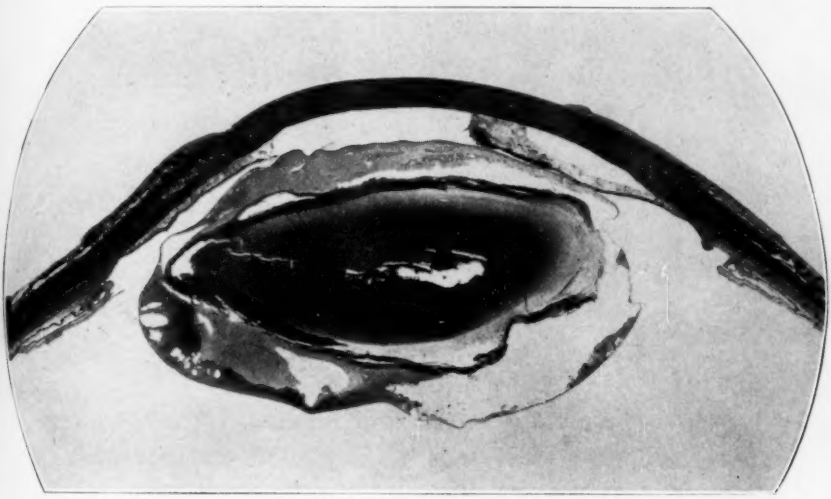


Fig. 4.—Recurrent uveitis; iris-lens adhesion. The iris and the lens are pushed forward. The anterior chamber is shallow. Glaucoma is present. Trephining without iridectomy was performed.

with glaucoma in both eyes and desquamation in one eye show consistently higher tension levels on the exfoliating side.

5. Secondary glaucoma may follow uveitis with adhesions of the iris to the lens capsule (iris bombé) sealing off the communication between the anterior and the posterior chamber. Secondary glaucoma produced by this route is clinically commonly seen. The lens usually participates passively. However, after iridectomy, in some cases in which there are old cyclitic cataract remnants, intermittent low grade uveitis and low tension, the inflammatory reactions are checked and after a digging out and removal of the remnants of the lens, some visual level returns. This procedure is hazardous to light perception and should be done only at a proper stage of the disease and with a full knowledge of the risks

involved. Nevertheless the point remains that removal of the remnants of the lens checks the inflammatory process. Rarely the tearing free of the posterior synechia by strong iris dilators pulls off part of the lens capsule and produces rapid swelling of the lens. In some intances a late stage shows the iris and the swollen lens pulled and thrust forward so that the anterior chamber is almost entirely obliterated.

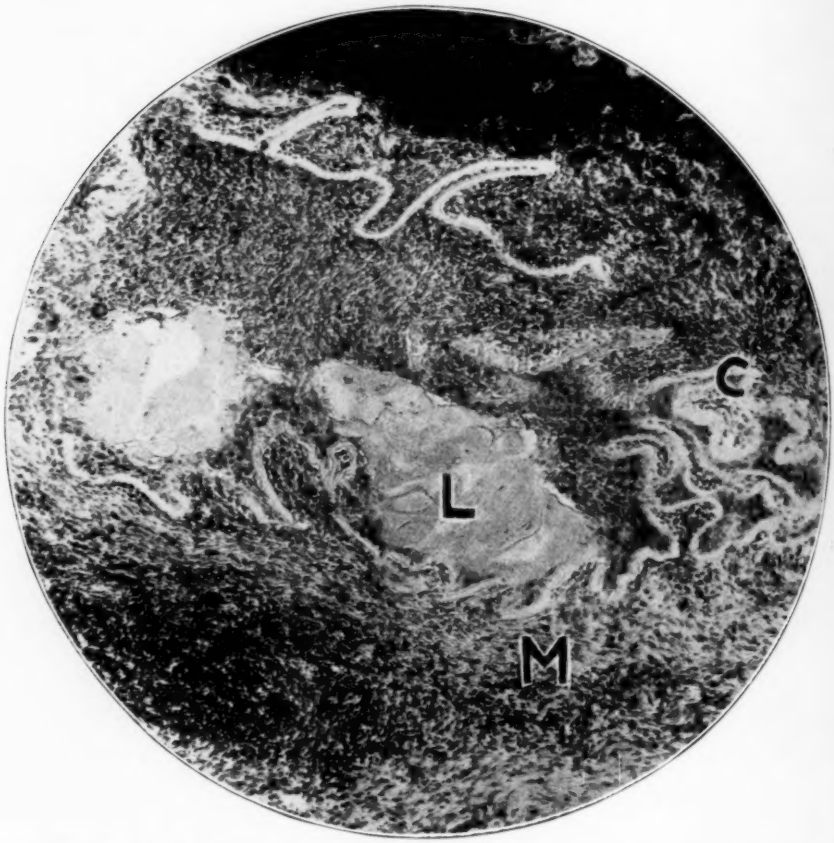


Fig. 5.—Penetrating wound; endophthalmitis phacoanaphylactica, later stage. The lens is largely destroyed. *L*, remnant of lens; *C*, folded capsule; *M*, inflammatory fibrous membrane.

6. The capsule may be opened sufficiently for the swollen lens material to block the angle mechanically. This is common after perforating wounds. Small amounts of lens cortex may also cause low grade secondary glaucoma due to toxic lens substance associated with uveitis.

7. Endophthalmitis phacoanaphylactica (Verhoeff and Lemoine[6]) may occur. The lens protein sensitizes the eye, producing usually a severe and sometimes (but more rarely) a milder inflammation, characterized by pus cells, macrophages, giant cells and liquefaction but no caseation necrosis. The reactions vary with the degree of sensitivity, the amount of lens matter that escapes and the position of the lesion—

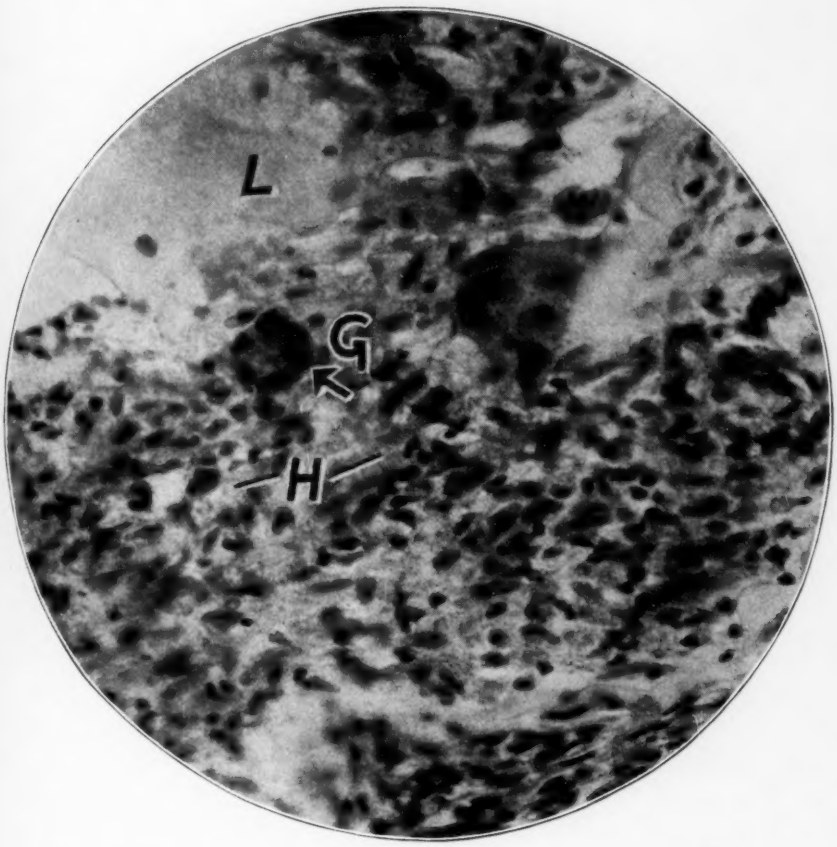


Fig. 6.—Higher power photomicrograph showing the cellular detail in a late stage of endophthalmitis phacoanaphylactica. *H*, histiocytes; *G*, giant cell; *L*, remnant of lens.

there is a greater reaction if this is posterior. There is an early tendency for the lens to become walled off by dense connective tissue. Although in adults there is abundant clinical evidence of specific reactions, as has been noted, in children there are discrepancies in the absence of this

6. Verhoeff, F. H., and Lemoine, A. N.: Endophthalmitis Phacoanaphylactica, Tr. Internat. Ophth. Cong., 1922, p. 234.

reaction. Some persons whose skin is sensitized to lens protein fail to show these ocular reactions in the presence of the cortical matter of extracapsular extraction. Burky and Woods [7] found that a suspension of lens protein aseptically produced was comparatively nontoxic. Burky [8] sensitized rabbits to beef lens and thus to their own lens pro-

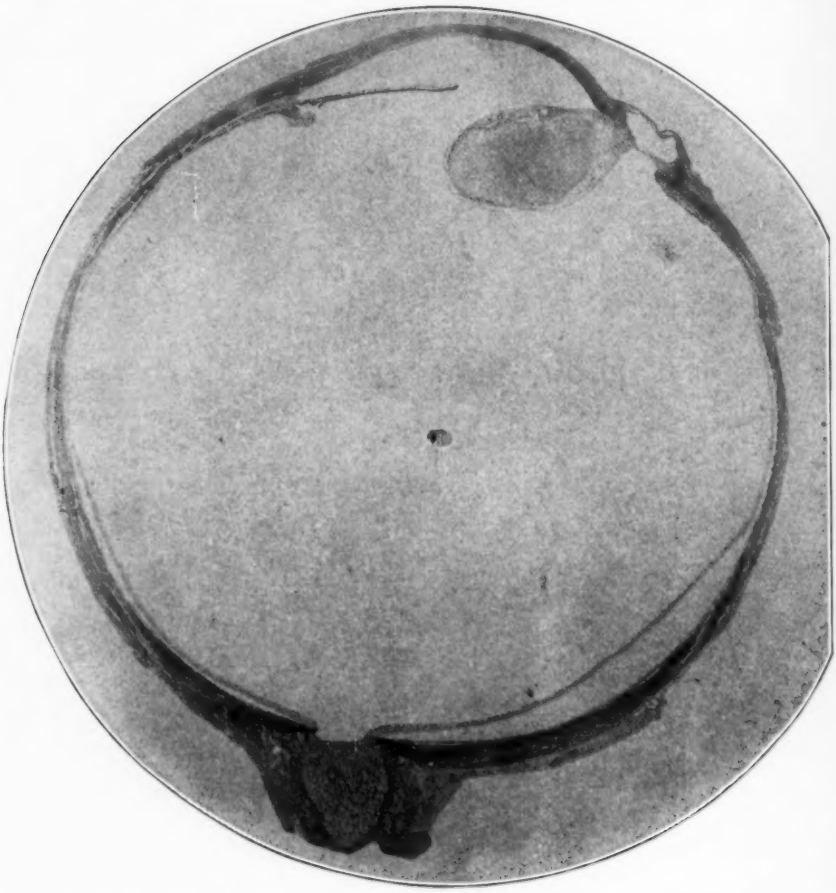


Fig. 7.—Congenitally (upward) dislocated lens; trephining operation.

tein. The animals showing a precipitin reaction to lens substance in high dilutions of blood serum gave severe endophthalmic reactions after minor traumas to the lens. Pathologically the experimental lesions

7. Burky, E. L., and Woods, A. G.: Lens Extract: Its Preparation and Clinical Use, Arch. Ophth. **6**:548 (Oct.) 1931.

8. Burky, E. L.: Experimental Endophthalmitis Phaco-Anaphylactica in Rabbits, Arch. Ophth. **12**:536 (Oct.) 1934.

resembled those seen in man. Burky was also able to desensitize (cutaneous reactions) by his lens extract, and the anaphylactic reaction did not follow opened lens capsules of the previously sensitized rabbits. The entity designated by Verhoeff and Lemoine, therefore, seems well established.

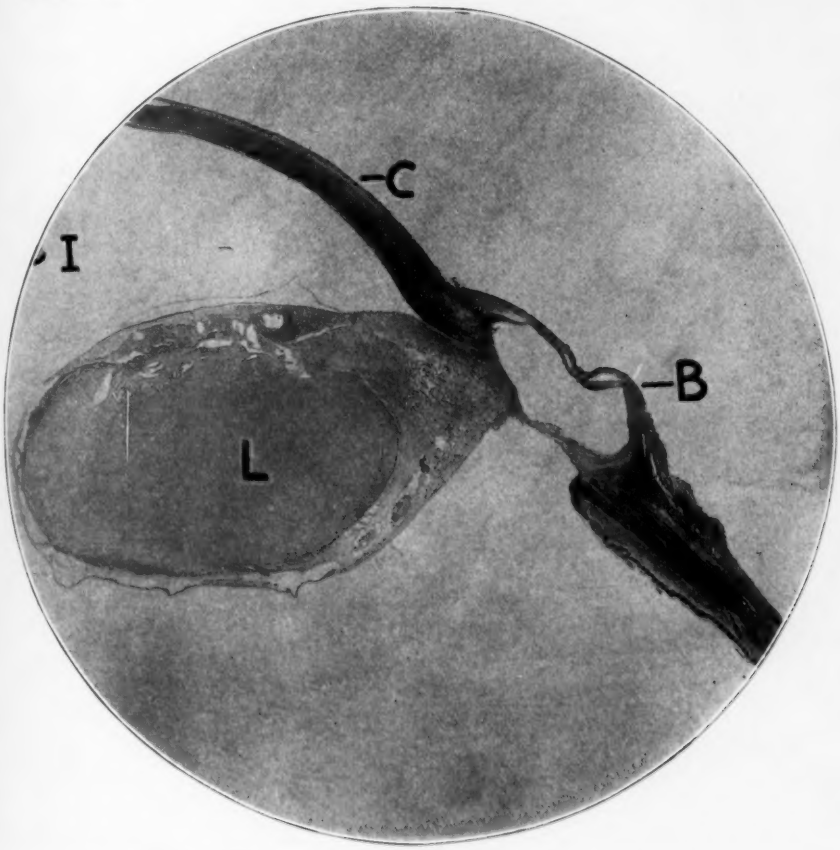


Fig. 8.—Higher power photomicrograph of figure 7. *C*, cornea; *I*, iris; *L*, lens; *B*, conjunctival bleb.

GLAUCOMA WITH THE LENS OUT OF POSITION

1. The lens may be partly luxated, owing to deficiency in the zonule (congenital ectopia); or there may be luxation of the congenital type, as seen in cases of arachnodactyly. This sometimes permits the lens to come in contact with the ciliary processes. Thus is produced an irritative vasomotor reaction in the ciliary processes, edema and perhaps increased permeability. The lens may be pushed forward and the angle of the anterior chamber partly blocked by the root of the iris against

the cornea. Rarely the patients may show attacks of segmental congestion of the globe over the ciliary ring. They sometimes respond paradoxically to miotics.

2. The lens may be tilted, partly out of its bed and in contact with ciliary processes due to trauma; but any mechanism which sufficiently relaxes the zonule, such as edema and lengthening of the ciliary processes, can make the tilting mechanically possible. This may at first be a very mild condition, with the chamber slightly irregularly deepened. The iris may or may not show some tremulousness in the quadrants.

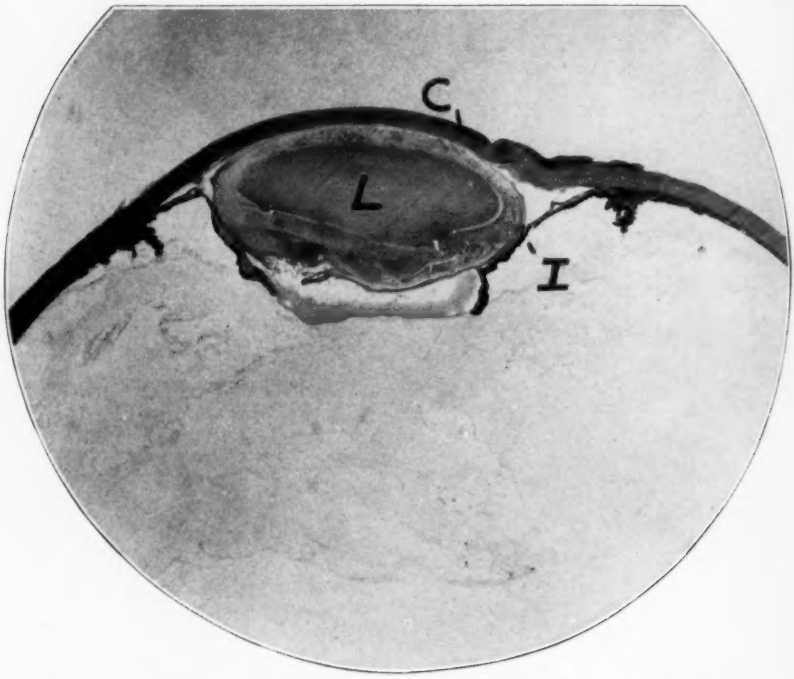


Fig. 9.—Lens dislocated into the anterior chamber; secondary glaucoma. *C*, cornea; *L*, lens; *I*, iris.

There is occasionally segmental congestion, like a mild scleritis, over the ciliary body, and with a widely dilated pupil and biomicroscopic methods one can sometimes confirm the tilt. The pupil is usually flattened on one side after dilation.

3. The lens may be luxated in the anterior chamber, blocking the pupillary space. This is usually due to trauma but is sometimes due to a weak zonule and a small lens. Glaucoma, as a rule, follows quickly.

4. The lens may be in the cornea (phacocele). This follows a perforating injury of the cornea, and there is usually rupture of the capsule.

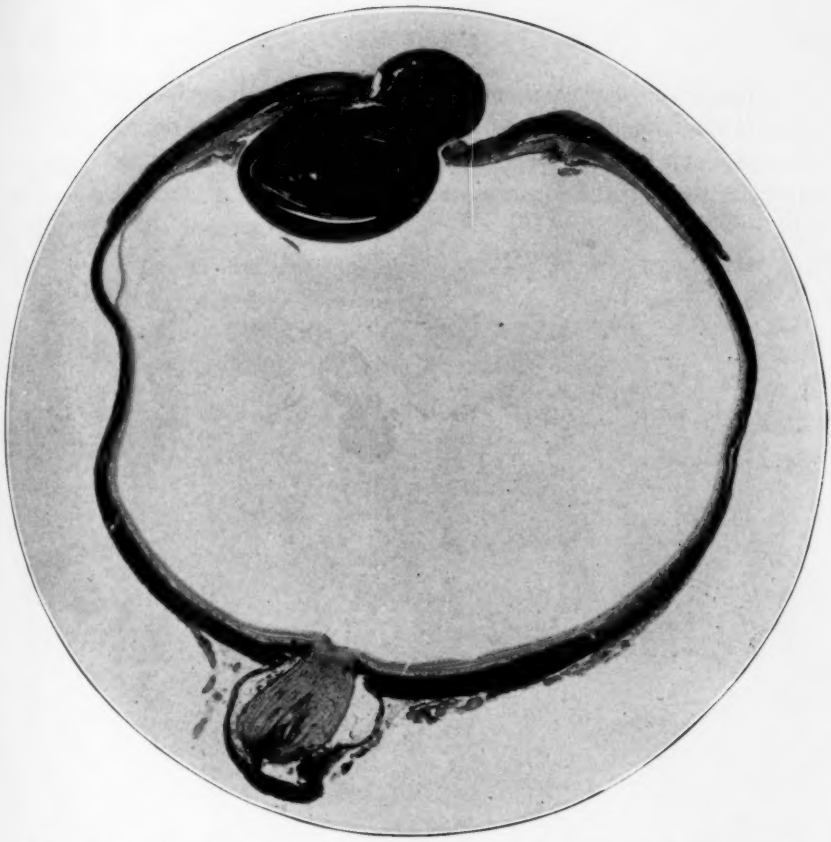


Fig. 10.—Lens, with capsule intact, prolapsed partly through the cornea; phacocele. The iris dragged forward and the anterior chamber obliterated.

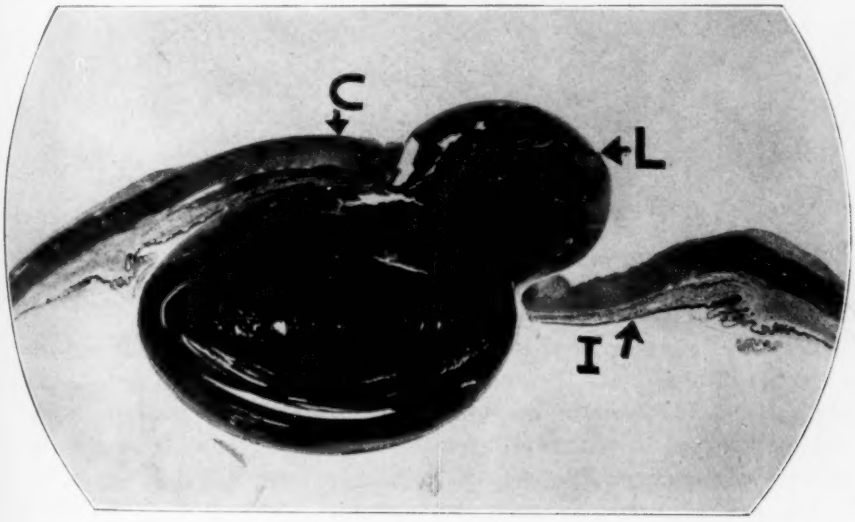


Fig. 11.—Higher power photomicrograph. *L*, lens; *C*, cornea; *I*, iris.

Occasionally the capsule is not ruptured. If it is ruptured, the presence of lens substance may cause glaucoma. If it is not ruptured, the iris may be swept across the angle. A most rare secondary glaucoma is produced by ingrowth of the epithelium associated with a corneal wound and phacocele.

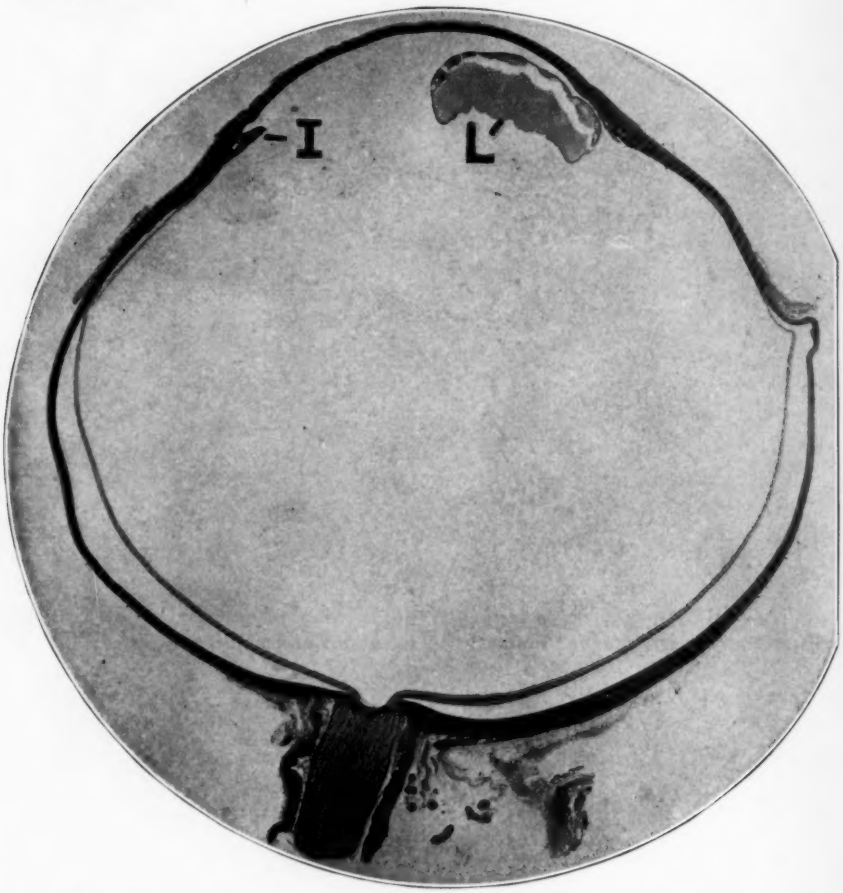


Fig. 12.—Large eye; small migratory lens; atrophied iris and ciliary body. The lens may go into the anterior chamber or drop back into the fluid vitreous. *L*, lens; *I*, atrophied iris.

5. The lens may be in the anterior part of the vitreous. When the lens lies on the ciliary ring, a foreign body cellular reaction is followed by formation of dense fibrous tissue that walls it off. The permeability of the capsule may increase; phagocytes and pus cells may enter the picture, and a fulminating form of uveitis may cause secondary glaucoma. In some eyes the anaphylactic reaction pattern is found.

6. The lens may remain in the posterior or in the central part of the vitreous for some time and may float about, producing low grade uveitis, foreign body reaction and sometimes secondary glaucoma. Rarely, without known trauma, a lens is spontaneously luxated in the large eye with fluid vitreous and an attenuated ciliary body. Such a lens may be small and rounded, with an ill developed ciliary body—the myopic eye. Its

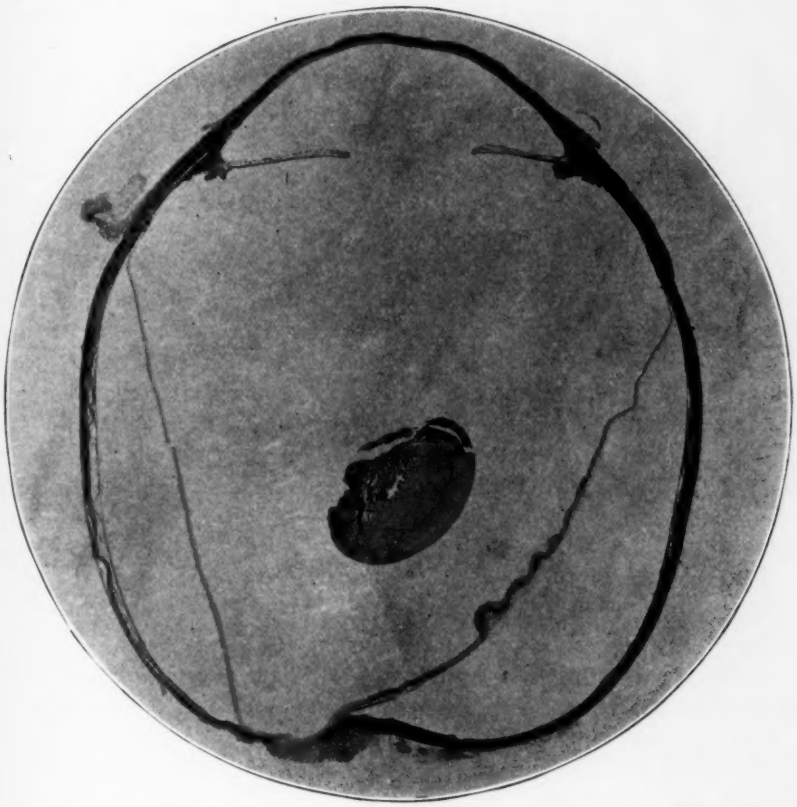


Fig. 13.—Large eye with fibrotic iris. The lens is luxated into the posterior part of the vitreous.

position, whether anterior or posterior, in some instances seems to relate to the structure of the iris.

7. The lens may lie against the retina or on the nerve head and may cause considerable congestion in the posterior quadrant of the eye. Ultimately the lens usually breaks down after permeability of the capsule is increased, and a very severe uveitis, with cellular influx, membrane formation and glaucoma, follows.

COMMENT

From what has been stated it may be seen that the lens is capable of causing glaucoma through a number of routes and also that the lens structure has within itself the material to produce glaucoma directly and indirectly. The lens may be said commonly to cause secondary glaucoma. Whether the lens initiates or merely accompanies the glaucoma complex clinically may not be determined. Even in the laboratory, priority of the pathologic process is sometimes difficult to establish. Once out of its bed, the lens becomes a marauder and is, in effect, a foreign body within the eye. The couched lens with an intact capsule usually causes uveitis, inflammatory cell infiltration, cell membrane formation and frequently secondary glaucoma. The uveitis, however, may be associated with hypotension, ocular disintegration and phthisis. In its bed the lens can initiate or participate in an inflammatory reaction leading to secondary glaucoma.

The tilted lens also is a potential destroyer. Since one is frequently able to follow the tilted or partly dislocated lens over a period of years without discovering the slightest evidence of glaucoma, suspicions may be lulled. It may be overlooked because of its chief by-product, glaucoma. Treating this form of secondary glaucoma apart from the lens gives unsatisfactory results.

The problem of diagnosis calls on every resource at the physician's command. The following signs and symptoms may be exhibited in part or in combination:

A history of previous similar trouble.

Trauma.

Familial ocular disease.

Recurrent congestion without known cause.

A partially tremulous iris which does not dilate evenly and is slightly flattened on one side.

Unequal pupillary response to light stimulus.

A slightly dilated pupil, with border atrophy and thin areas; ectopic pupillary border pigment.

Segmental congestion over the ciliary body, resembling mild scleritis; rarely, a thin area of congestion in the sclera.

Alteration of the depth of the anterior chamber.

Bands across the filtration angle, visible by use of the gonioscope.

Inconsistent refractive errors due to forward position and tilting of the lens.

Pigment on the corneal endothelium and on the lens capsule.

Cells in the anterior chamber.

Desquamation of the lens capsule seen before and after dilation of the pupil. The edge of the lens and some evidence of the zonule layer of capsule separation may be seen with a widely dilated pupil.

Asymmetry of the postlental space.

Elevation of the intraocular tension (not always present).

Changes in the visual fields (not always present). Provocative tests for glaucoma may help to classify such changes.

SUMMARY

A classification of secondary glaucoma due to abnormalities of the lens has been outlined. Trauma is the predominating background of luxation of the lens (of the 45 globes studied in the laboratory, there was a history of trauma in about 90 per cent). Taking a long range view and considering the likely course of events, one feels that conservative treatment calls for removal of the lens when tilting or partial luxation is seen in association with inflammatory changes. A lens sharply luxated or weakly suspended should be removed. This is indicated definitely when there are recurring attacks of ocular pain, moderate inflammatory changes and perhaps increase in tension with no other cause demonstrable. In such circumstances the glaucoma is sometimes treated by iridectomy or trephining. The logical approach is to remove the lens. Some patients can carry the partially tilted lens for many years without resulting inflammation and visual deterioration if the intraocular tension is not destructively raised over the ample threshold of the filtration angle.

ABSTRACT OF DISCUSSION

DR. SANFORD R. GIFFORD, Chicago: Dr. Heath has covered such a tremendous territory in this review that I do not wish to discuss his whole paper but shall merely add a note on one type of glaucoma secondary to changes in the lens which I have been interested in ever since my father showed me its occurrence a number of years ago. It seems to be one with which many ophthalmologists are not familiar. Dr. Heath has spoken of it, and it is the type in which the intact hypermature lens produces a low grade uveitis which seems to be accompanied frequently by a moderate increase in intraocular tension. It is the same type of glaucoma which occurs with so-called serous iritis. I encounter a case about once in every two or three years. I just happen to have observed a typical case—that of a man who has had a hypermature cataract. The pupil has been white for ten years. About two weeks ago he came to the hospital with low grade uveitis; the tension was 35 mm. of mercury, and there were a few precipitates on the posterior surface of the cornea and some cells in the anterior chamber. The tension was reduced temporarily by miotics and then increased again. Removal of the lens, as Dr. Heath has stated, brings relief in such cases. I do not wish to go into the question of endophthalmitis, as to whether it should be called endophthalmitis phacogenetica or phacoanaphylactica. It is my opinion that endophthalmitis phacoanaphylactica is somewhat rare and that endophthalmitis due to absorption of broken-down lens material, which one has to think of as amino acids, which cause a chemical reaction in the eye, is more frequent. The whole lens protein is not absorbed through the capsule, as a rule. The result of the removal of the lens, especially when it can be removed in the capsule by Verhoeff's method, with complete iridectomy, has been satisfactory in the few cases in which I have used it.

EFFECT OF THYROXIN ON INCIPIENT SENILE CATARACTS

DAVID F. GILLETTE, M.D.
SYRACUSE, N. Y.

Hope and a limited understanding of ocular metabolism prompted the empiric use of numerous drugs [1] in an attempt to check the development and cause the absorption of the opacities of incipient senile cataracts.

The failure of these remedies, together with an increasing knowledge of the physiology of the endocrine glands, stimulated the use of glandular preparations in ophthalmic research and practice.

Van Zandt [2] described the visual disturbances incident to cataracts in his cases and attributed the temporary improvement in visual acuity to his endocrine therapy. He concluded that dysfunction of the thyroid was the activating agent, while dysfunctions of the gonads and of the pituitary were adjuvants, in the production of the senile opacities of the lens.

Kerr and his associates [3] reported some success following the oral use of thyroid substance for senile cataract.

Kirby [4] administered parathyroid extract to a group of selected patients with cataract and reported, as did Cargill [5] a year later, that there was no improvement in the lens opacities.

Hoesch [6] and Klemens [7] expressed the opinion that parathyroid extract checks the further development of lens opacities but has no effect on those already present.

---

1. Pollock, W. B.: The Treatment of Early Opacities in the Senile Lens, Glasgow M. J. **99**:32-51 (Jan.) 1923. Siegrist, A.: Der graue Alterstar, Berlin, Urban & Schwarzenberg, 1928.

2. Van Zandt, L. L.: Influence of Endocrines on Lenticular Opacities, Texas State J. M. **19**:286-288 (Sept.) 1923.

3. Kerr, W. J.; Hosfored, G. N., and Shepardson, H. C.: Treatment of Senile Cataract with Thyroid Extract, Endocrinology **10**:126-144 (March-April) 1926.

4. Kirby, D. B.: Senile Cataract: The Use of Parathyroid Extract, Arch. Ophth. **5**:754-759 (May) 1931.

5. Cargill, L. V.: The Management and Treatment of Incipient Cataract, Canad. M. A. J. **24**:400 (March) 1931.

6. Hoesch, K.: Cataract and Parathyroid Epilepsy, Deutsche med. Wchnschr. **63**:1582-1585 (Oct. 15) 1937.

7. Klemens, F.: Cataract and Hypofunction of Parathyroid, Deutsche med. Wchnschr. **65**:753-754 (May 12) 1939.

Siegrist [8] developed an extract of the combined endocrine glands called paraphakin (euphakin) and used it in a series of patients with senile cataracts. He reported an improvement in visual acuity but did not note any modification of the opacities.

Von Köteles [9] claimed that euphakin checks the development of cataracts but does not alter the opacities present.

Peters [10] reported some favorable results following the use of euphakin and iodides for senile cataracts.

Wolfe and his associates [11] stated that the use of thyroid, iodides and other alteratives is of unquestionable value in the treatment of senile cataracts.

Löwenstein [12] expressed the opinion that glandular extracts do not cause absorption of the lens opacities in most instances. He reported the use of thyroidin (an extract of sheep thyroid), pluriglandular extracts and ovarian extract. He mentioned as an exception the cataract of diabetes, which, he said, reacts favorably to injections of insulin.

Sanderson [13] claimed that the topical use of iodides enhances the effect of mixed glandular therapy for incipient cataracts.

Mura [14] stated that the senile cataract results from the failure of the endocrine system in general and from dysfunction of the thyroid, hypophysis and adrenals in particular.

Kleiber,[15] on the other hand, found normal function of the thyroid in patients with senile cataracts.

Jameson,[16] who had used thyroxin, the active principle of the thyroid, for 25 patients with senile cataract, expressed the belief that the clinical evidence substantiates the hope of its effectiveness as a local metabolic stimulant and alterative.

---

8. Siegrist, A.: Pathogenesis and Medicinal Therapy of Senile Cataract, Ann. d'ocul. **169**:696-703 (Sept.) 1932.

9. von Köteles, M.: Favorable Results with Euphakin, Klin. Monatsbl. f. Augenh. **87**:70-73 (July) 1931.

10. Peters, A.: Medicinal Treatment of Senile Cataract, Fortschr. d. Therap. **7**:179-183 (March 25) 1931.

11. Wolfe, O.; Wahrer, F. L., and McLeod, J.: Non-Surgical Treatment of Cataract, Eye, Ear, Nose & Throat Monthly **11**:76-79 (March) 1932.

12. Löwenstein, A.: Histologic Aspects of Cataract Due to Disturbances of Organs of Internal Secretion, Arch. f. Ophth. **132**:224-238, 1934.

13. Sanderson, D. D.: Non-Surgical Treatment of Cataract, Nebraska M. J. **21**:216-219 (June) 1936.

14. Mura, F.: Etiology of Senile Cataract: Role of Endocrine Dysfunction, Boll, d'ocul. **14**:526-548 (April) 1935.

15. Kleiber, G.: Role of Thyroid in Development of Senile Cataract, Arch. f. Augenh. **105**:704-709, 1932.

16. Jameson, P. C.: Use of Thyroxin in Ophthalmology, Arch. Ophth. **12**:635-643 (Nov.) 1934.

Burden-Cooper [17] later supported this opinion.

This clinical study of the effect of the topical use of synthetic thyroxin (1 cc. equivalent to 2 mg.) on incipient senile cataracts was accompanied with animal experimentation with the assistance of Dooley.[18] It consisted of instillation of the thyroxin into the conjunctival sacs of healthy adult rabbits twice daily over periods of from two weeks to five months and subconjunctival injection of 1 cc. of the solution into the eyes of additional rabbits. The aqueous was then withdrawn with a hypodermic syringe and examined for iodine. The findings were all negative for iodine content above 0.005 mg. The test used demonstrated its presence in solutions known to contain iodine in dilutions as low as 0.005 mg.

It was shown in the University of Rochester School of Medicine and Dentistry (department of physiology, hygiene and nutrition) that the instillation of thyroxin into the conjunctival sacs of 3 rabbits was followed by a prompt rise in the energy metabolism. The investigators assumed but did not attempt to prove that the solution passed through the lacrimal ducts and was swallowed rather than absorbed from the conjunctival sac.[19]

Eighteen of the 20 patients in this investigation had uncomplicated binocular senile cataracts and were otherwise in good physical condition. In most of the cases the opacities were of the incipient type, and the knowledge of their presence was kept from the patients. These patients were taught to instil one or two drops of synthetic thyroxin (1 cc. equivalent to 2 mg.) into each eye morning and night and immediately put pressure over the puncta. This prevented the rapid passage of the drug into the nasopharynx and at the same time allayed the local irritation.

Groat [20] advised against recording the basal metabolic rates of these patients in cases of senile cataract. He argued that the changes, if any, would be so small as to be within the normal variations according to the clinical tests used and so would be of no scientific value.

The visual acuity, both corrected and uncorrected, together with sketches of the objective lens findings, were recorded, and the records were repeated at intervals throughout the course of treatment. A study of a group of these records showed that the intraocular tension was not uniformly altered by the thyroxin therapy.

The visual acuity was dependent on the position of the opacities and remained good so long as a central portion of the lens remained

17. Burden-Cooper, J.: Non-Surgical Treatment of Cataract, Glasgow M. J. **130**:109-134 (Sept.) 1938.

18. Dooley, M. S.: Personal communication to the author.

19. Murlin, J. R.: Report of the work done for this investigation.

20. Groat, W. A.: Personal communication to the author.

TABLE 1.—*Data on Treated Patients*

Patient	Sex	Age	Visual Acuity Before Treatment: Uncorrected	Visual Acuity Before Treatment: Corrected	Time Thyroxin Was Used, Mo.	Visual Acuity After Treatment: Uncorrected	Visual Acuity After Treatment: Corrected	Comment
1	F	59	R 20/200+ L 18/200	20/20+ 20/20+	49	20/70+ 10/200	20/20— 20/20—	R, lens opacities increased little; L, lens opacities increased more
2	M	57	R 20/30— L 20/20—	20/30+ 20/20	23	20/20 20/30	20/20 20/20—	Lens opacities increased in size and density
3	F	69	R 2/200 L 20/40+	20/100 20/20—	32	L.P. 10/200	L.P. 10/200	R. contusion cataract with secondary glaucoma; L, immature cataract (patient had a psychosis)
4	F	58	R 10/200 L 10/200	20/20— 20/20—	22	10/200 10/200	20/20— 20/20—	Opacities little changed; increased little in size and density; still peripheral
5	F	72	R 20/200+ L 20/30	20/30+ 20/30	21	20/70— 20/200+	20/30+ 20/50+	Opacities increased slightly
6	F	66	R 10/200 L 10/200	20/30+ 20/30+	27	10/200 10/200	20/30—2 20/30	Opacities increased in size and density
7	F	72	R 20/40— L 20/100	20/25+ 20/30+	22	20/25+ 20/100	20/20 20/30	Opacities progressively increased
8	F	66	R 20/100 L 20/40	20/25 20/25	11	20/50— 20/30—	20/30— 20/30+	Opacities increased
9	M	60	R H.M. L 20/200	H.M. 20/30—	48	L.P. 12/200	L.P. 20/50	R, hypermature cataract; faulty projection; L, opacities gradually increased
10	F	77	R 5/200 L 6/200	5/200 20/200	17	L.P. 20/200	L.P. 20/200	R, successful cataract extraction; L, immature cataract; thyroxin discontinued after extraction of right lens
11	F	62	R 4/200 L 20/40+	20/30+ 20/20	40	1/200 20/50	20/30 20/20—	Opacities increased; right lens slightly swollen (patient died)
12	F	62	R 20/200 L 18/200	20/30+ 20/30—	57	20/200 20/200	20/25+ 29/30—	Lens opacities increased in size and density
13	F	65	R 10/200 L 5/200	20/50+ 20/50	27	10/200 5/200	20/50 20/50+	Opacities increased; nuclei more sclerosed
14	F	58	R L.P. L 20/100	L.P. 20/40	24	L.P. 5/200	L.P. 20/70	Opacities continued to develop during period of treatment (patient died)
15	F	54	R 20/70 L 20/70+	20/30— 20/30—	49	20/100+ 20/40—	20/30 20/30—	Opacities increased peripherally
16	M	71	R 20/40+ L 20/50	20/20— 20/20—	13	20/50 15/200	20/25 20/200	Opacities increased, more rapidly in left lens
17	F	70	R 20/200+ L 20/200	20/30— 20/40—	23	20/200 20/200	20/40 20/50	Opacities progressively increased
18	F	63	R 20/100 L 20/70	20/25+ 20/25+	47	20/70 20/100	20/40— 20/40	Opacities increased in size and density
19	F	66	R 20/200 L 20/100+	20/100 20/70	15	20/70 20/100	20/70+ 20/50+	Opacities increased in number, size and density
20	M	62	R 20/200 L 20/200	20/25 20/40	40	20/200 20/200	20/30 20/30	Opacities increased in density

H.M. indicates hand movements; L.P., light perception.

TABLE 2.—*Data on Control Subjects*

Patient	Sex	Age	Visual Acuity First Visit: Uncorrected	Visual Acuity First Visit: Corrected	Period of Observation	Visual Acuity Now: Uncorrected	Visual Acuity Now: Corrected	Comment
1	F	51	R 20/100+ L 20/100+	20/30+ 20/20	4 yr.	20/100 20/100	20/20+ 20/20+	Opacities increasing slowly peripherally
2	F	67	R 10/200 L 20/100	10/200 20/20+	16 mo.	5/200 20/70+	5/200 20/15+	Opacities slowly increasing, R more than L
3	F	56	R 20/20+ L 20/20—	20/15+ 20/15+	13 yr.	20/30+ 20/25+	20/20 20/20	Lens opacities increased very slowly (peripherally)

clear. The patients with striae or clefts in the lens complained of blurred vision in bright light even though the visual acuity was good. The cataracts in all these cases became more central as the size and density of the opacities continued to increase.

The untreated control subjects also showed a very slow progression of the incipient lens opacities.

CONCLUSIONS

1. Thyroxin used locally does not check the development of senile lens opacities.

2. Thyroxin does not cause absorption of the lens opacities already present.

3. Thyroxin does not have any demonstrable local metabolic effect.

4. Visual acuity alone is not an index of the progress of incipient senile cataracts.

TREATMENT OF ANGIOMATOSIS RETINAE

HERBERT KAYE, F.R.C.S., D.O.M.S., D.T.M.& H., R.C.P.& S.
JOHANNESBURG, SOUTH AFRICA

In the February 1940 issue of the ARCHIVES, Cordes and Hogan [1] advocated the use of roentgen therapy in the treatment of retinal tumors occurring in association with von Hippel's disease. They reported some improvement. Cordes and Hogan also stated that localized radium therapy in cases of early involvement produces a greater effect on the tumor mass than does roentgen irradiation, thus suggesting radium therapy as the method of choice. The use of radon seeds near the ora serrata may cause irradiation cataract and, in some cases, grayish white exudates at the macula appearing a year after irradiation.

I should like to advocate a method that has been completely successful in the cases of 2 young persons afflicted with this disease. The mother of the patients is blind in both eyes as the result of angiomatosis retinae with the usual end picture of complicated cataracts and detachments; she has been given radium treatment, with no success. The eldest son has, I understand, a "paralysis" but refuses ocular examination. My patients are another son, aged 24, and a daughter, aged 26.

REPORT OF TWO CASES

The daughter had a blind right eye with a complicated cataract and had been unsuccessfully treated with radiation therapy. Vision in the left eye when she was first examined, in 1938, was 6/6; in the temporal periphery of the retina there showed the typical picture of an angiomatous tumor—a sharply demarcated red globular mass, rather whiter over the middle portion, fed by an enlarged tortuous artery and drained by an engorged companion vein. There was also slight elevation of the surrounding retina. There were no other abnormalities in the fundus, and the macula and the vitreous were perfectly healthy.

The son showed an identical picture except that the condition was less advanced; he had no complaints about his eyes, and it was only through routine examination that a small tumor was discovered. This growth was fairly flat and red, the whole area looking the size of a small coin, such as a sixpence, but giving the impression of being baglike; the usual enlarged artery and vein were present. The vision was 6/6.

It was important to make an attempt to save the young woman's only eye, and with this end in view I sent both the brother and the sister to London, England. During July Mr. H. Stallard operated on the two tumors. He treated the growths by a combination of katholysis and surface diathermy; katholysis was used for localization of the growth, and then the katholysis needle was passed into and around the large feeding vessels just proximal to the growth. The growth itself was

1. Cordes, F. C., and Hogan, M. J.: Angiomatosis Retinae (Hippel's Disease): Report of Case in Which Roentgen Therapy Was Used in Early Stage, Arch. Ophth. **23**:253-269 (Feb.) 1940.

treated by katholysis punctures of 3 milliamperes for three seconds; three applications of surface diathermy (100 milliamperes for eight seconds) were made over the site of the growth, and this was followed by several punctures with a 1.5 mm. needle (40 milliamperes for three seconds). In the technic it is important to mark the site of the localizing punctures on the sclera with gentian violet or by a touch with the electrocautery, as the puncture hole is very small and on review of the sclera after ophthalmoscopic examination is often very difficult to detect. The katholysis punctures should be made 0.25 to 0.5 mm. apart and should be sufficient in number to cover the whole area of the growth. It is essential to demarcate the limits of the neoplasm first and then to fill in the center of this space by punctures; unless this is done, some of the hydrogen bubbles mask the ophthalmoscopic view of the neoplasm and it is difficult to tell by this means whether all the growth has been adequately treated. Very fine sharp platinum needles are required for penetration; there is a slight risk of hemorrhage into the vitreous when perforating needles are used. The sister did have a slight hemorrhage into the vitreous which soon cleared.

I have now followed these 2 cases for twelve months and can report a completely satisfactory result, with full preservation of vision; the brother's eye has been protected from a certain retinal detachment which usually follows enlargement of the growth, and the sister has been saved from certain blindness. The previously enlarged vessels running to each island of the growth are now normal in size; the eye shows the larger area of choroidal destruction, and the area formerly occupied by the tumor is densely white, with a good deal of fibrous tissue, which makes it difficult to focus the area, owing to the unevenness of the surface. There is the well known area of pigmented atrophy surrounding the growth, as seen after the usual diathermy operations for retinal detachments. The retinal vessels in the treated area are very pale and are sclerosed from fibrosis. The choroidal vessels are also sclerosed, but there are no abnormal tortuous vessels to be seen. Similarly, the brother's retinal tumor has completely disappeared, and in its place is a finely pigmented, flattened area with complete absence of tortuous vessels.

I removed the girl's blind eye recently, as it had become painful; there is undoubted shrinking of the conjunctiva, with chronic redness due to previous radiation treatment. Slight attacks of giddiness were reported to me on her last visit, and naturally I am watching for any suggestion of cerebellar involvement.

The treatment described is thus to be recommended for the solitary type of vascular tumor characterized by a single nodule located far forward; the essence of the treatment is to produce obliterative endarteritis of the large dilated quadrant branch of the retinal artery which feeds the yellowish gray mass of angiomatous tissue and also of the companion vein. The variety marked by hemispheric crimson swellings like balloons on a string or resembling renal glomeruli is likely to be accompanied with multiple retinal lesions, such as tortuous and convoluted arterioles, glial masses, cysts and hemorrhages into the retina and the vitreous.

There is always the possibility that fresh tumors may form in these 2 cases. If this takes place the indication will be for immediate obliteration of the feeding vessels by katholysis, treatment of the growth by katholysis and, if thought necessary, by use of surface diathermy and even diathermy punctures.

THE NEW SCOTOMETER

JOHN N. EVANS, M.D.
BROOKLYN

The progress of scotometry has in my opinion been materially retarded by the lack of a simple and inexpensive instrument. While it is admitted that the ideal scotometer probably cannot be devised, still the inadequacy of the simple models available and the expensiveness of the more complete instruments leave a gap which can be bridged. I have endeavored to meet this need by designing the instrument about to be described.

In developing the presented instrument, every effort was made to minimize manufacturing costs in an effort to keep the retail price as low as possible. The dimensions were so selected as to permit the use of standard equipment and to make unnecessary departure from the generally accepted technic.

Thus, the illuminating system was designed about a standard, commercial "show case," light bulb. The cord, connector and light switch are standard products. The tangent surface was so proportioned that it could receive plotting charts already on the market, and the standard fixation distance of 190 mm. was adopted. The rims of the columnating lenses were so proportioned and designed as to permit the attachment of trial case lenses and such accessories as prisms, color filters and obturators (occluders).

An effort was made to maintain the utmost simplicity of structure but at the same time to provide for the addition of such accessories as would permit conversion of the instrument from a monocular scotometer to the standard form of stereocampimeter by the simple addition of a second columnating lens, a dividing partition and the necessary prisms from the trial case.[1] Provision for the addition of mirrors, macular

---

The National Electric Instrument Company assisted in the development of this instrument.

From the Department of Ophthalmology, Long Island College Hospital and the Long Island College of Medicine.

Demonstrated at the Seventy-Sixth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 4, 1940.

1. To simplify construction and manipulation, it has been found advantageous to employ a spheroprism (+ 5.25 sph. = 3.00 degrees) combination for the columnating lens. The trial case lenses are then used for the correction of the refractive error.

selectors and a variety of testing charts was also included in the basic design, with the idea that ultimately a greater number of diagnostic aids could be evolved.

A great deal of thought was given to the selection of a pattern for the plotting chart. The conclusion was finally reached that any convenient arbitrary design would have as much scientific significance as the most elaborate calculations. One cannot apply to a tangent surface any mathematically derived universal pattern which will apply to a particular eye under clinical study.

In an effort to avoid the introduction of an entirely new plotting background, the standard pattern used on the Lloyd slate was adopted. Lloyd suggested that the first 5 degrees near the fixation point occupy 16.3 mm. of chart. Such a pattern does not, of course, answer all objections, but it seemed more desirable than a new pattern, which might be ideal for a schematic eye only. Objection had been made to the hexagonal pattern of the Lloyd slate on the grounds that it interfered with the use of minute objects. Though this objection is only theoretic and not found to exist in practice, this pattern has been omitted from the new slate.

Since this instrument is basically a scotometer, it is not essential that the effect of a third dimension be produced. Hence, one will find that the chart provided gives only superposition of the images as seen by the right and the left eye. Available standard charts can, however, be used in this instrument with perfect third dimensional effect.

A series of very light concentric circles was adopted as the simplest pattern to encourage monocular fixation. The problem of fixation in scotometry is much more complicated than one might suspect, as will be obvious after reference to a previous contribution.[2]

In order to permit the examiner to use his own judgment in this controversial subject, a simple fixation guide was adopted. Figure 1 shows the small central circle at the center of the chart, with four heavier centrally projecting spokes. This results in a fixation "spot," characterized by detail of form, for observation of which the macula is physiologically fitted. This figure can be supplemented by tracing it with a white wax pencil, or it may be rendered less conspicuous by shading with a lead pencil. (It will be recalled, however, that decrease in definition of form and brightness may encourage fixation by that part of the retina most responsive to poor detail and dim light—eccentric retina.)

DIAGRAMS OF BLINDSPOTS

I have long felt that the diagrams of blindspots as found on most plotting charts were not appropriate for scotometry with minute objects.

2. Evans, J. N.: An Introduction to Clinical Scotometry, New Haven, Conn., Yale University Press, 1938.

It is obvious, however, that the examiner must not limit himself in a particular case by any arbitrary standard.

Nevertheless, it seemed necessary that the subject be reviewed. Dr. Charles Hopkins undertook this tedious task.[3] His conclusions are adopted as the most suitable measurements for the presented plotting chart.

The paper on which this background pattern was impressed is not theoretically perfect. Every attempt has been made to secure a smooth yet uniformly dead black paper which would receive a pale gray design. It is difficult to secure such a paper the nap of which does not entangle

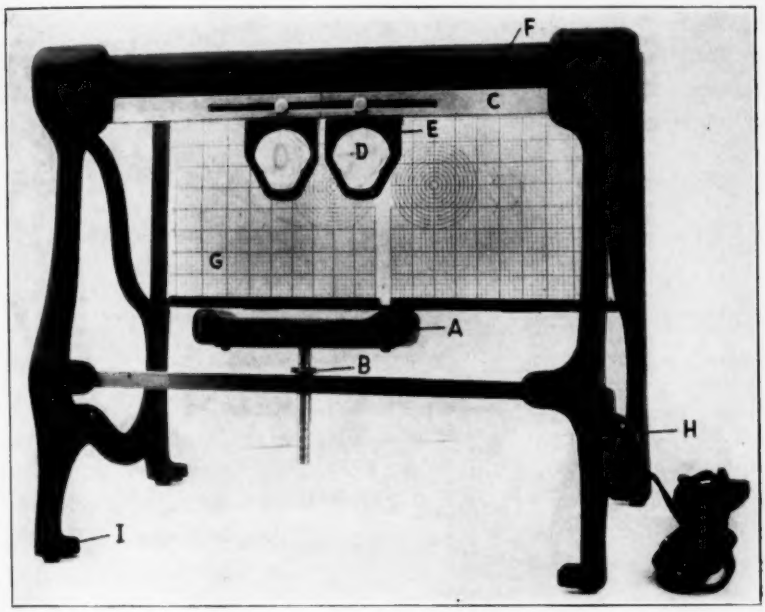


Fig. 1—The scotometer when used as a binocular instrument (middle partition removed in this illustration in order to make chart visible). *A*, wide chin rest, only necessary to adjust height. *B*, height-adjusting nut. *C*, brow bar, forehead rest; the slot permits setting interpupillary distance. *D*, columnating lens; it has an engraved central circle to aid in centering subject's eye. *E*, lens rim, with small protruding lugs or tongues to retain trial case lenses and accessories and with small elevated ridge for sighting, to aid in centering subject's eye. *F*, housing: reflector covering built about a standard "show case" light bulb. *G*, note plotting chart with fixation figures, concentric circles, 1 degree squares and outlines of blindspot and angioscotoma "stumps." *H*, switch. *I*, feet are provided with rubber cups and screw holes for securing scotometer to table top. The back of the chart carrier serves as a receptacle for the supply of charts.

3. Hopkins, C.: To be published.

the minute objects. The so-called velour paper is almost ideal, but its cost is prohibitive. One chart is sufficient for both eyes when the instrument is used monocularly, as the pattern of the blindspot of the right eye is placed on one side and that of the left eye is placed on the reverse side. A stereoscopic chart embodying the aforementioned features for use when the instrument is employed as a stereocampimeter was also designed for use.

OBJECTS

In an effort to provide the ideal object appropriate for use with this instrument, it was found necessary to construct two forms. Theoretically it would seem best to use only minute disk-shaped objects of paper thickness, but objects of this character cannot be consistently made or measured for commercial production by any method which has come to my attention. The objects as originally described were made of filamentous silver wire, fused at one end into minute spheres, the wire stem

Blindspot Measurements as Suggested for Use with Small Objects at One Hundred and Ninety Millimeters (Hopkins[3])

Region Measured	Macula to Nasal Border	Width of Blindspot	Macula to Temporal Border	Area, Scotoma Units	Above Horizontal	Below Horizontal	Vessel Stump 1 Degree from Border of Blindspot		Object Size, Mm.
							Above	Below	
Average in mm.....	44.1	25.8	69.9	12	7.3	19.6	4.2	4.0	0.68

being blackened with india ink and the sphere whitened by immersion in hydrochloric acid. Dr. Henry Abbott[4] has described satisfactory spherical objects which he makes by fusing droplets of white shellac or sealing wax on the end of filamentous black tungsten wire. While these are practical and satisfactory for individual manufacture, they do not lend themselves to commercial production. Hence, it has been found necessary to devise a means of mounting minute opaque white porcelain or glass spheres on black tungsten wire. It is possible to make these as small as 0.4 mm., and the following sizes are advocated: 0.4 mm., 0.6 mm., 1 mm. and 1.5 mm. They are mounted in black fiber handles and after thorough trial seem admirably adapted for the mapping of the angioscotoma and minute central field defects of all types.

A series of disk-shaped objects supplements this set, in the following sizes: 2 mm., 4 mm. and 6 mm. The disks are 0.5 mm. to 0.25 mm. in thickness and are made of brass and properly blackened on the stem, and one face, the opposite face of the disk, which is used for testing, has

4. Abbott, H.: To be published.

a roughened finish similar to the finest grade of sandpaper. This permits the application of chalk of any color desired and guarantees the permanence and reproducibility of the test surfaces. Should one desire to renew or change the color of the surface, it is only necessary to rub the surface with a small stiff brush before applying the new finish of chalk.

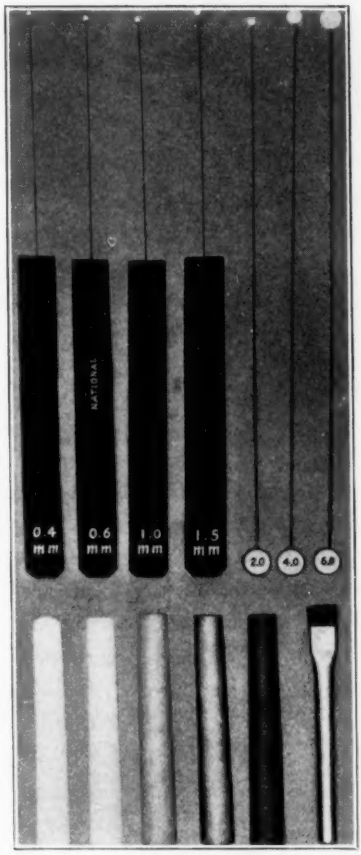


Fig. 2.—The two forms of objects are illustrated as described in the text. Below, there are five sticks of chalk in white and carefully selected colors. The brush is used to remove the chalk from the roughened surface of the disk-shaped objects when one wishes to apply a different color.

It will be noted that there is little in the way of innovation in the present device and accessories. The main interest in the presentation of the new scotometer is an attempt to produce an instrument which is as inexpensive as possible but also accurate.

VITAMIN B IN OPHTHALMOLOGY

CLARENCE A. VEASEY JR., M.D.
SPOKANE, WASH.

The vitamin B complex is a group of water-soluble substances necessary in minute quantities for health and growth in man and in other animals. Some of these substances have been identified chemically; the existence of others is predicated on disease in laboratory animals fed deficient diets. At present the following components have been identified or are presumed to exist:

Thiamine (or vitamin B_1) is the antineuritic and beriberi-preventing vitamin. It acts as a catalyst in the combustion of carbohydrate, which in its absence is arrested at the pyruvic acid stage, the metabolite having a toxic effect on nerve tissue. Thiamine deficiency in man causes a noninflammatory peripheral neuritis and paralyses, but not nerve degeneration. The neuritis is most apt to occur in the presence of noxious substances, such as alcohol, an elevated concentration of blood sugar or the toxins associated with toxemia of pregnancy. Gastrointestinal symptoms, including hypermotility, hypomotility and anorexia, have been frequently described, but there is no specific lesion of the gastrointestinal tract. Dysfunction of the bowel may cause insufficient absorption of vitamin B_1 even if the dietary intake is adequate. With severe deprivation there are enlargement of the right side of the heart, palpitation and dyspnea, and with less severe deficiency there may be changes in rhythm and in the electrocardiogram. The edema of thiamine deficiency is not of renal or cardiac origin. There are many suggestions of a relation to the endocrine glands. Thiamine is useful in large doses to combat roentgen ray sickness and may control the pain of tic douloureux. There is some clinical evidence of benefit to allergic persons from its use.

The normal limits of elimination of thiamine in the urine have been determined and used as a laboratory guide in the diagnosis of deficiency. Most of the determinations are biologic; a few are chemical, but none is sufficiently simple or reliable for routine clinical use.

Condensed from a candidate's thesis submitted to the American Ophthalmological Society in August 1939. For a full discussion of the chemistry and the general clinical and experimental aspects of vitamin B, with bibliography, the reader is referred to the original article in the Transactions of the American Ophthalmological Society for 1940.

The body requirement of thiamine is related to the weight and to the caloric intake. For the average adult the minimum amount required to prevent beriberi is about 300 international units, or 1 mg. of thiamine hydrochloride per day, while for optimum health about five times as much should be ingested. Therapeutic doses up to 500 mg. or more of thiamine hydrochloride may be given without untoward symptoms, but it must be remembered that there is little storage, so that large doses do not lead to useful retention. A dose of 25,000 mg. is not toxic.

Riboflavin (vitamin G, or B_2) combines in the body with a protein to form a ferment which is concerned with cell respiration. Its absence leads to degeneration of central and peripheral nerve tissue, keratitis and cataract formation in laboratory animals. Its exact role in human nutrition is not known, but lack of it, in association with thiamine deficiency, is apparently responsible for the degenerative changes of beriberi. A syndrome called cheilosis has been attributed to it, and there is clinical evidence that it is related to some forms of keratitis and swelling of the lens. The daily requirement for man is probably 2 to 3 mg., and the substance is not toxic in many thousand times this amount.

Nicotinic acid is the pellagra-preventing (P-P) factor in human beings and the anti–blacktongue factor in dogs. Its deficiency in man is also apparently responsible for certain psychotic states. In conjunction with thiamine it is related to perceptive deafness in some cases. In cases of pellagra the pathologic picture is dependent on associated deficiencies of thiamine and riboflavin. Nicotinic acid deficiency causes photosensitivity leading to dermatitis from sunlight. Human requirements are unknown, but the maintenance dose is over 200 mg. per week. Five hundred milligrams per day has been given, but toxic symptoms, such as flushing, burning and itching of the skin and gastrointestinal disturbances, occur.

Vitamin B_6 has been isolated and identified [1] as pyridoxine and has been synthesized. Its deficiency in the rat causes a specific dermatitis, including loss of hair about the eyes, and in the dog and pig, microcytic hypochromic anemia. Its role in human nutrition is unknown.

The remaining factors of the vitamin B complex have not been isolated and are known only by the effect of their absence from the diet of experimental animals. The following data have been obtained:

Vitamin B_3 is necessary for growth and appetite in pigeons.

Vitamin B_4 prevents a specific paralysis in rats and is necessary for chicks.

Vitamin B_5 prevents loss of weight in pigeons.

The filtrate factor (factor 2, chick antidermatitis factor, precipitate factor of Elvehjem) is the vitamin B complex with thiamine, riboflavin

1. The chick factor is pantothenic acid. Its absence causes atrophy of the adrenal cortex, gonads and auditory nerve.

and vitamin B_6 removed. It obviously contains nicotinic acid. It is concerned with dermatoses in chicks, blacktongue in dogs and pellagra in man and contains Morgan's gray hair–preventing factor.[1]

There are eight other factors mentioned in the literature. These are of doubtful existence or factors of which little is known.

Gross deficiency disease is not commonly seen in ordinary ophthalmic practice, but owing to the refinement and storage of foods, especially the milling of grains, and the use of sugar for a great part of the caloric intake, a large section of the population, including the well-to-do, has a daily ingestion of vitamin B not far above the level associated with frank beriberi. The parish poor in England in 1782 received almost twice as much as do the best families today.

Classic B-avitaminotic states may be recognized by the gross dietary errors and the clinical symptoms, but it is difficult to summarize the picture of subclinical avitaminosis B. The patient is below par and is easily labeled "neurasthenic." He is easily fatigued and is subject to flatulence, fulness and hypermotility or hypomotility of the gastrointestinal tract. He has a rapid pulse without fever or hyperthyroidism and may have palpitation, dyspnea and unexplained edema. He is probably nervous, possibly with vague mental symptoms; he is subject to headaches and may have neuritis. There may be evidence of endocrine imbalance, especially of an underactive thyroid and gonadal insufficiency. He is apt to be slightly deaf to high pitches, owing to involvement of the eighth nerve. He may be allergic and slightly anemic. It is said that elderly women are most apt to be deficient, and I should add allergic persons who have been on restricted and unbalanced diets.

OCULAR PHYSIOLOGY AND DISTRIBUTION OF THIAMINE AND RIBOFLAVIN

Data concerning the ocular physiology and distribution of vitamin B are few and uncorrelated. Fischer [1a] analyzed beef lenses and found thiamine present to the amount of 0.001 microgram per lens but was unable to demonstrate thiochrome (a photosensitive oxidation product of thiamine). He stated that thiamine is absent in cataractous lenses, which disturbs the glucoside metabolism and allows accumulation of pyruvic acid, which characterizes progressive opacification of the lens. Referring to the general physiologic role of thiamine as demonstrated by Peters, this explains the paucity of lactic acid in cases of cataract.[2] Offret [3] expressed the belief that thiamine acts on the neurosensory apparatus of the eye and possibly on the motor apparatus also.

1a. Fischer, F. P.: Presence of Vitamin B_1 in the Lens and Its Significance, Arch. d'opht. **2**:108 (Feb.) 1938.

2. Fischer, F. P.: Aneurin (Vitamin B) in the Lens, Ophthalmologica **96**: 219 (Jan.-Feb.) 1939.

3. Offret, G.: Avitaminoses and Their Relation to the Visual Apparatus, Rev. méd. franç. **19**:135 (Feb.) 1938.

Fischer (cited by Buschke [4]) has shown that riboflavin is present in normal lenses, that it decreases with advancing age and that it is wholly absent in cataractous lenses, having become lumiflavin by a process of photolysis against which it is protected in normal lenses. He expressed the belief that it acts as a dehydrating ferment or oxido-reduction system, rendering possible the occasionally necessary ferment metabolism in the lens. Yudkin [5] stated the belief that riboflavin is one of the essentials for health of the lens. Van Heuven [6] stated that it is necessary in the lens for the conduction of light. Hogan [7] stated that 0.2 to 0.4 microgram of riboflavin is present in the human eye (about one hundredth of that found in the codfish eye) and that it may possibly enable eyes to perceive shorter wavelengths by converting them to green. Rachevski [8] stated that the yellow color of the human lens is partly due to riboflavin and that this substance is also present in the aqueous, having to do with lenticular respiration. Kodičkova-Hradečka and his co-workers [9] reported a reduction in lenticular ascorbic acid in rats deficient in the vitamin B complex.

Von Euler and his co-workers, cited by Buschke,[4] demonstrated a green fluorescent flavin in the retinal pigment epithelium of fishes, rabbits, cattle, human beings and albinotic mammals. The substance is free or only loosely bound in the tissue and is transformed into lumiflavin under the influence of light. The riboflavin activity of the retina corresponded to the amount of this substance present. There was great variation in the amount of the flavin, and it seemed to have no relation to preliminary illumination; so the authors doubted that it had any relation to visual function. Van Heuven stated that riboflavin is present in large quantities in the retina but did not elucidate its function. Fleischmann and Pichler [10] have demonstrated the return of respiration in retinas poisoned with a cyanide after the addition of riboflavin. Adler

4. Buschke, W.: Vitamins in Ophthalmology, Ztschr. f. Vitaminforsch. **5**:37, 1936.

5. Yudkin, A. M.: Diet and Vitamins in Relation to Cataract, Am. J. Ophth. **21**:871 (Aug.) 1938.

6. Van Heuven, J. A.: Vitamins in Ophthalmology, Geneesk. gids **16**:798 (July 22) 1938.

7. Hogan, A. G.: Riboflavin: Physiology and Pathology, J. A. M. A. **110**: 1188 (April 9) 1938.

8. Rachevski, F. A.: Vitamin Therapy in Ophthalmology, Vestnik oftal. **10**:63, 1937.

9. Kodičkova-Hradečka, J.; Joachim, J., and Kodicek, E.: Cevitamic Acid and Glutathione and Morphologic Findings in Lens of Guinea-Pig with Deficiency of Vitamins B and C, Časop. lék. česk. **76**:1553 (Sept. 3) 1937.

10. Fleischmann, W., and Pichler, E.: Riboflavin: Influence on Tissue Respiration of Brain and Retina, Klin. Wchnschr. **17**:314 (Feb. 26) 1938.

and von Euler [11] demonstrated riboflavin in the retinal pigment of fish in a concentration twenty-five times that found in the liver. They pointed out that it is found free and not combined with a protein as an enzyme, as is usual in animal tissues. Free riboflavin is found only in the eye, in milk and in urine. They suggested that it may be important in the eye because of its fluorescence and photosensitivity, and Offret [3] stated the belief that it has to do with lenticular respiration.

EXPERIMENTAL AND CLINICAL EVIDENCE OF OPHTHALMIC VITAMIN B DEFICIENCY

It is noteworthy that the textbooks on general medicine make little mention of ocular conditions in the B avitaminoses, despite the fact that beriberi and pellagra have been recognized for a long time. It may possibly be that the severe general symptoms diverted attention from the eyes or that the patients were not ophthalmologically examined. In Osler's "Principles and Practice of Medicine," [12] Meakin's "Practice of Medicine" [13] and Cecil's text [14] there are no ocular symptoms mentioned under beriberi or pellagra. In "Oxford Medicine" there are listed no ocular symptoms of beriberi, but mention is made of ocular changes in a current insert on pellagra, a condition which will be mentioned later. There is little in the ophthalmic texts, except in that of Fuchs,[15] who gave pellagra as a cause of cataract, and in that of Berens,[16] who mentioned beriberi as a cause of retrobulbar neuritis and oculomotor lesions.

A review of the experimental and clinical ophthalmic literature led Buschke to summarize the ocular symptoms of beriberi as: (1) corneal and conjunctival changes and (2) changes in the optic nerve. The symptoms of pellagra are optic neuritis, diplopia, hemeralopia, keratomalacia, cataract, atrophy of the optic nerve, glaucoma and constriction of the retinal vessels. Foster,[17] however, stated that cataract is not part of the pellagra syndrome, and Offret [3] said that beriberi is seldom accompanied with ocular disorders.

---

11. Adler, E., and von Euler, H.: Lactoflavin (Riboflavin) in Eyes of Fish, Nature, London **141**:790 (April 30) 1938.

12. Osler, W.: Principles and Practice of Medicine, revised by H. A. Christian, ed. 13, New York, D. Appleton-Century Company, Inc., 1938.

13. Meakins, J. C.: Practice of Medicine, St. Louis, C. V. Mosby Company, 1936.

14. Cecil, R. L.: A Textbook of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1937.

15. Fuchs, E.: Text-Book of Ophthalmology, ed. 7, Philadelphia, J. B. Lippincott Company, 1923.

16. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936.

17. Foster, J.: Vitamins in Ophthalmology, Proc. Roy. Soc. Med. **29**:755 (May) 1936.

As the clinical problem of a given patient begins with the determination of the existing ocular defects rather than the knowledge of a specific dietary deficiency, I shall consider seriatim the various structures of the eye and their possible involvement resulting from avitaminosis B.

Lashes, Conjunctiva, Cornea.—In thiamine-deficient pigeons Katajama observed photophobia and epiphora associated with dryness and anemia of the conjunctiva and corneal opacity with impaired sensitivity.[4]

Alopecia and falling lashes usually occur in riboflavin-deficient rats,[18] and sanguinopurulent conjunctivitis occurred in O'Brien's series. Dor concluded that edema of the lids, alopecia and keratoconjunctivitis should be considered as due to riboflavin deficiency when they are associated with cataract.[4]

In the reports of experimental production of cataracts in rats on riboflavin-deficient diets by Day, Langston and O'Brien [19] (1931) and by Langston, Day and Cosgrove [20] (1933), keratitis was mentioned as a prominent symptom; it occurred in about three quarters of the animals and preceded the changes in the lens by about two weeks. This was confirmed in a similar series in 1938.[21] Bessey and Wolbach,[22] in similar experiments, noted corneal vascularization in a month, with turbidity due to leukocytic infiltration appearing later. On administration of riboflavin the turbidity disappeared in two days and the vessels in two weeks. They stated that a similar condition occurs in cases of avitaminosis A and ascribed it to asphyxia of the corneal epithelium.

Clinically, edema of the lids is reported in cases of beriberi. Maintland suggested that phlyctenular keratoconjunctivitis may be due to deficiency of vitamin B, as it frequently clears after correction of a diet high in refined starches, and Milhaud suggested that styes may have a similar cause because of the efficacy of administration of yeast.[8] Grosz [23] assumed that in the presence of diseases of the lids and phlyctenulosis avitaminosis A is also present, but he recommended the use of riboflavin for the last-named condition.

---

18. Day, P. L.; Darby, W. J., and Langston, W. C.: Identity of Flavin with Cataract-Preventive Factor, J. Nutrition **13**:389 (April) 1937.

19. Day, P. L.; Langston, W. C., and O'Brien, C. S.: Cataract and Other Ocular Changes in Vitamin G Deficiency, Am. J. Ophth. **14**:1005 (Oct.) 1931.

20. Langston, W. C.; Day, P. L., and Cosgrove, K. W.: Cataract in Albino Mouse Resulting from Deficiency of Vitamin G (B_2), Arch. Ophth. **10**:508 (Oct.) 1933.

21. Day, P. L.; Darby, W. J., and Cosgrove, K. W.: Arrest of Nutritional Cataract by Use of Riboflavin, J. Nutrition **15**:83 (Jan.) 1938.

22. Bessey, O. A., and Wolbach, S. B.: Vascularization of the Cornea of the Rat in Riboflavin Deficiency with a Note on Corneal Vascularization in Vitamin-A Deficiency, J. Exper. Med. **69**:1 (Jan.) 1939.

23. Grosz, S.: The Importance of Vitamin B in Ophthalmology, Arch. f. Ophth. **140**:149, 1939.

Keratomalacia has been reported in cases of pellagra [4] (due to associated vitamin A deficiency?). Yudkin [24] described a more or less distinct type of sluggish corneal ulceration, resistant to or made worse by the usual therapeutic measures, which responds to vitamins A and B. He also reported 16 cases in which patients with keratitis were apparently benefited by large doses of cod liver oil and vitamin B complex, but he did not consider the corneal changes specific. Koepcke [25] also recommended vitamins A and B for the treatment of corneal ulcers. Suurkula [26] reported a case of rodent ulcer in a woman aged 49, with improvement after twelve intragluteal injections of thiamine hydrochloride. Takeda observed superficial keratitis in association with riboflavin deficiency.[4]

Thiamine has been used successfully by Nitzulescu and Triandaf [27] in 2 cases of herpetic keratitis. Injections of 6 mg. of thiamine hydrochloride daily for five days produced a cure. Grosz [23] stated that thiamine acts as a soothing agent in this condition, and Koepcke [25] recommended it as a useful adjunct. Buschke [4] stated that Aguyao observed changes of the corneal epithelium, apparently due to involvement of the trigeminal nerve, in the last months of pregnancy, complicated by beriberi, and that Marchesini and Papagno observed corneal hypesthesia in association with this disease.

Kruse and his co-workers [28] reported 9 cases of cheilosis and keratitis in which the symptoms cleared on administration of riboflavin and returned when diets deficient in this vitamin were given. In 2 additional cases of interstitial keratitis in congenitally syphilitic patients there was marked improvement with riboflavin therapy. This is most interesting in view of the well known necessity of building up the general health in persons with congenital syphilis and the lack of brilliant response to antisyphilitic therapy alone.

Lens.—In 1931 Day, Langston and O'Brien [19] observed the occurrence of cataract in 45 of 48 albino rats on a riboflavin-deficient diet. The accompanying symptoms were alopecia, sanguinopurulent conjunctivitis and interstitial keratitis. The lenticular opacities were

24. Yudkin, A. M.: Vitamins in Treatment and Prevention of Ocular Diseases, Arch. Ophth. **19**:366 (March) 1938.

25. Koepcke, G. M.: Vitamins and Infections of Eye, Nose, Throat and Sinuses, Journal-Lancet **57**:460 (Oct.) 1937.

26. Suurkula, J.: Is Rodent Ulcer of the Cornea to Be Attributed to a Deficiency of Vitamin B_1? Klin. Monatsbl. f. Augenh. **102**:500 (April) 1939.

27. Nitzulescu, J., and Triandaf, E.: Treatment of Herpetic Keratitis with Vitamin B, Brit. J. Ophth. **21**:654 (Dec.) 1937.

28. Kruse, H. I.; Sydenstricker, V. P.; Sebrell, W. H., and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis, Pub. Health Rep. **55**:157 (Jan. 26) 1940.

nuclear, anterior and posterior, subcapsular and cortical; they failed to progress after administration of riboflavin and did not develop if even minute traces were in the feed. The lenses were amorphous, with morgagnian globules, and showed degeneration of the lens fibers with proliferation of the epithelium. In 1933 Langston, Day and Cosgrove [20] conducted similar experiments on 47 animals, with the following morbidity:

Keratitis in 79 per cent after forty-three days
Cataracts in 96 per cent after forty-eight days
Ophthalmitis in 57 per cent after fifty days

In 1938 Day and his associates [21] reported cataracts appearing in fifty-two days in 13 of 16 riboflavin-deficient rats. The cataracts proceeded to maturity in 75 per cent of the animals in sixty-seven days. The average period of survival was seventy-four days. Twenty-five rats with incipient cataracts were fed 120 micrograms of riboflavin twice a week, with the following results:

In 11 rats the cataracts were arrested in both eyes.

In 6 rats the cataracts were arrested in one eye, those in the other eye proceeding to maturity.

In 2 rats the cataracts proceeded to maturity.

In 6 rats the lenses were clear after the keratitis cleared.

This experiment showed conclusively that riboflavin was the substance involved and that arrest would occur when it was restored to the diet. Day and Darby [29] demonstrated an inverse relation between growth and the incidence of cataract in these animals, but, as Kodičkova-Hradečka [9] found no lenticular opacities in 14 rats starved to death, the changes cannot be attributed to inanition. In lactose and galactose cataracts, such as those produced by Yudkin and Arnold [30] and others, Mitchell and Cook [31] showed that neither thiamine nor riboflavin play a part.

Tainter and Borley [32] were unable to produce cataracts in riboflavin-deficient rats even with the addition of dinitrophenol. The animals

29. Day, P. L., and Darby, W. J.: Inverse Relation Between Growth and Incidence of Cataracts in Rats Given Graded Amounts of Vitamin-G-Containing Foods, J. Nutrition **12**:387 (Oct.) 1936.

30. Yudkin, A. M., and Arnold, C.: Cataracts Produced in Albino Rats on Ration Containing High Proportion of Lactose or Galactose, Arch. Ophth. **14**: 960 (Dec.) 1935.

31. Mitchell, H. S., and Cook, G. M.: Galactose Cataracts in Rats: Factors Influencing Progressive and Regressive Changes, Arch. Ophth. **19**:22 (Jan.) 1938.

32. Tainter, M. L., and Borley, W. E.: Influence of Vitamins and Dinitrophenol on the Production of Experimental Cataract, Arch. Ophth. **20**:30 (July) 1938.

without the poison lived an average of sixty-eight days (extreme, one hundred and seventy-three days), which is well over the necessary time for lenticular changes. Ahmad and Guha [33] were unable to produce cataracts in rats by riboflavin deficiency and expressed the opinion that some other factor of the vitamin B complex, as well as individual susceptibility, is involved.

In regard to these failures and György's negative experimental results, Day and his associates [18] stated that only very minute amounts of riboflavin are necessary to prevent cataract formation, and he examined five casein preparations (two of which are commercial and in common use), both chemically and biologically and found traces of riboflavin present.[34] They expressed the belief that failures to produce cataracts are due to impure casein preparations. However, in an experiment [35] in which he utilized small amounts of cheese to provide traces of riboflavin in the diet, cataracts still occurred and relatively large amounts of cheese were necessary to prevent the specific lenticular change.

Experience with cataracts in man has given much less conclusive results. There are no reports to show that persons with cataracts are deficient in riboflavin, and there is nothing to demonstrate that riboflavin deficiency in the human species has an effect similar to that observed in the rat. Derkač [36] reported on 7 patients with senile cataracts treated with subconjunctival injections of vitamin C and intramuscular injections of riboflavin. He stated that after several months "satisfactory results" were obtained in 2 cases and expressed the belief that incipient cataract can be helped but not cured. Yudkin [37] reported that in many cases intumescence of the lens can be reduced by administration of 2 teaspoons of potent yeast powder and the juice of two lemons daily before meals. There was no improvement after striae were present. I had 1 patient with incipient senile cataract in whom the progressive swelling of the lens was apparently arrested by riboflavin given parenterally and vitamin B complex given by mouth. The peripheral

33. Ahmad, B., and Guha, R. C.: Some Observations on the Experimental Production of Cataract, Indian J. M. Research **25**:547 (Oct.) 1937.

34. Day, P. L., and Darby, W. J.: Influence of Different Casein Preparations in Riboflavin-Deficient Diet upon Appearance of Cataract, Biochem. J. **32**:1171 (July) 1938.

35. Day, P. L., and Darby, W. J.: Cataract Preventive Vitamin (Flavin) in Cheese, Food Research **1**:349 (July-Aug.) 1936.

36. Derkač, V.: Medical Treatment in Senile Cataract: Report of Cases, Klin. Monatsbl. f. Augenh. **100**:226 (Feb.) 1938.

37. Yudkin, A. M.: Diet and Vitamins in Relation to Cataract, Am. J. Ophth. **22**:308 (March) 1939.

opacities did not change. Laval [38] advised thiamine and riboflavin therapy for incipient cataract and expressed preference for yeast tablets because of the sulfur content, there being some possible connection between the sulfur content of fish lenses and the prevention of human cataract, as reported by Shropshire, and between cystine and galactose cataracts in rats.

Wagner, Richner and Karbacher [39] treated 11 patients (21 eyes) with riboflavin for six to seven months, the slit lamp findings being recorded by drawings every month. One group received two tablets daily of riboflavin and the second group 1 cc. of 0.5 per cent solution of riboflavin administered intravenously. The results were as follows:

Vision		*Slit Lamp Findings*
4 eyes	Unchanged	9 eyes
10 eyes	Improved	0 eyes
7 eyes	Worse	12 eyes

In all cases of subcapsular cataract there was an increase in the opacity, an unchanged appearance on slit lamp examination being observed only with other types of cataract. The authors pointed out that subjective improvement of vision is not a reliable criterion. They concluded emphatically that riboflavin is not efficacious in the treatment of cataract. It is to be regretted that the refraction was not observed for a decrease or an absence of increase in minus correction, in view of Yudkin's observations regarding intumescence. Moreover, the tablets specified by the authors are not listed in the manufacturer's catalogue; so the actual dose given by mouth is unknown. The intravenous dose was 5 mg. per day, which is only double the daily requirement. This cannot be considered adequate therapeusis if the subjects were in need of riboflavin saturation. Without some kind of laboratory estimate to demonstrate deficiency of vitamin B in the cases studied the experiment proves only that the visible opacities in cataracts selected at random do not improve under mild riboflavin therapy.

I must agree with Foster [17] that there is nothing convincing in clinical experience concerning riboflavin and cataracts.

Optic Nerve.—Experimental work on the optic nerve has been conducted for the most part on pigeons with beriberi.[4] Barlatta examined the optic nerves and tracts from such birds and found histologic swellings and interruptions of the myelin sheaths. These occurred with

38. Laval, J.: Vitamin Therapy in Ophthalmic Practice, Am. J. Ophth. **22**:33 (Jan.) 1939.

39. Wagner, H.; Richner, H., and Karbacher, P.: Cataract Therapy by Administration of Vitamin B_2 (Riboflavin) Controlled by Slit Lamp Microscopy: Preliminary Results, Klin. Monatsbl. f. Augenh. **101**:543 (Oct.) 1938.

greater frequency than in normal controls. Katajama noted degeneration of the myelin sheaths and thickening of the axis-cylinders of the optic nerves, which was not present if vitamin B had been given. Marchesini and Papagno noted ascending fatty degeneration of myelin in the chiasm and in the optic nerves, particularly in the maculopapular bundle, where many axis-cylinders appeared slightly swollen. Fazio was unable to confirm any of these findings, and Bertrand, Liber and Randoin reported no abnormalities of the optic tract in cases of experimental B avitaminosis. These experiments were probably not conducted on animals with uncomplicated beriberi (riboflavin deficiency), as nerve degenerations do not occur in this condition, and the negative results in the last two groups may have been due to traces of riboflavin in the diets.

From the clinical standpoint there is much more evidence concerning the optic nerves than there is concerning cataracts. Although Offret [3] said that ocular disorders are seldom associated with typical beriberi, there are many case reports tending to show that retrobulbar neuritis is not uncommon in association with avitaminosis B. The reports, however, are frequently not clear as to whether the general condition is a deficiency of one factor or of the entire complex.

As long ago as 1929, Shastid [40] reported 2 cases of optic neuritis of undiscoverable cause in which prompt remission of symptoms followed large doses of the vitamin B complex in the form of wheat germ extract in 1 case and yeast in the other. Shastid pointed out, however, the fallacy of assuming "post hoc, ergo propter hoc." Soriano and Puiggari [41] reported a single case of retrobulbar neuritis associated with beriberi in which the diagnosis was made on the basis of a history of malnutrition and exclusion of other causes, involvement of the optic nerve being the only symptom. In 1935 Soga reported an outbreak of so-called beriberi amblyopia (now known to be chronic retrobulbar neuritis) in Japan, including 7 personal cases, in 2 of which, without vitamin therapy, the patients recovered just as well as those in the remaining 5, who received vitamin B.[4] In their clinical studies of beriberi Marchesini and Papagno noted retrobulbar neuritis with central scotoma and temporal or total pallor of the optic disk.

Fine and Lachman [42] reported on 3 pellagrins with cutaneous lesions in whom retrobulbar neuritis without cecocentral scotomas occurred. Kyrlov found impaired vision in about one third of his patients with

40. Shastid, T. H.: Two Cases of Optic Neuritis Treated with Vitamin B, Am. J. Ophth. **12**:903, 1929.

41. Soriano, F. J., and Puiggari, M. I.: Retrobulbar Neuritis Due to Beriberi, Arch. de oftal. de Buenos Aires **13**:244 (May) 1938.

42. Fine, M., and Lachman, G. S.: Retrobulbar Neuritis in Pellagra, Am. J. Ophth. **20**:708 (July) 1937.

pellagra, with temporal pallor and constriction of the finer vessels.[4] Laval [38] stated that the optic neuritis associated with pellagra is cured by yeast. Probably also pellagrinous were the conditions first described by Moore [43] in 1930 and again reported by him in 1937.[44] He described a syndrome occurring among Nigerians, observed in 60 per cent of 3,000 persons with ocular disease and manifested by reduced vision, photophobia, sore tongue, white patches at the edges of the lips and a dry, scaly, itchy scrotum. Almost two months after the onset temporal pallor of the disk appeared, later leading to primary atrophy of the optic nerve. Occasionally optic neuritis was noted. Syphilis and yaws were excluded serologically. The patients were cured by marmite (vegex) and autoclaved yeast, and therefore the conditions were presumably due to deficiency of flavin or of nicotinic acid. The author stated that, no matter how spectacular the recovery, there are always some residual visual defects. A similar syndrome has been reported by others from Africa, Jamaica, the Solomon Islands, Sierra Leone, Barbados and Malaya.

Dymling [45] reported a series of 27 cases of optic neuritis, in most of which there was a slightly elevated white cell count with lymphocytosis, which he attributed to deficiency of vitamin B. Wagener and Weir's [46] postoperative observations might come in this class, as well as the involvement of the optic nerve sometimes seen in cases of Wernicke's syndrome.[47] The last two conditions may be identical.

There is considerable evidence to show that toxic amblyopia occurs by the action of the poisons on optic nerves when the threshold has been lowered by avitaminosis B.[23] Yudkin [48] first called attention to this connection in 1933, when he reported having obtained cure of amblyopia due to alcohol and tobacco by giving a diet rich in vitamins without

43. Moore, D. G. F.: Nutritional Retrobulbar Neuritis Followed by Partial Optic Atrophy, Lancet **1**:1225 (May 22) 1937.

44. Moore, D. G. F.: Retrobulbar Neuritis cum Avitaminosia Followed by Post Partial Optic Atrophy—Now Shown to Be of Pellagrinous Nature: Its Serious Incidence and Its Need for General Investigation, West African M. J. **9**:35 (June) 1937.

45. Dymling, O.: Contributions to the Clinic of Optic Neuritis, Acta ophth. **16**:547, 1938.

46. Wagener, H. P., and Weir, J. F.: Ocular Lesions Associated with Post-Operative and Gestational Nutritional Deficiency, Am. J. Ophth. **20**:253 (March) 1937.

47. Ecker, A. D., and Woltman, H. W.: Wernicke's Disease: A Neuro-Ophthalmic Syndrome of Nutritional Deficiency, Proc. Staff Meet., Mayo Clin. **14**:520 (Aug. 16) 1939.

48. Yudkin, A. M.: Ocular Disturbances Produced in Experimental Animals by Dietary Changes: Clinical Manifestations, J. A. M. A. **101**:921 (Sept. 16) 1933.

stopping the use of the noxious substances. In 1937 Carroll [49] reported a similar cure in 7 of 8 cases when yeast was added to the diet. The following year the same author, in collaboration with Goodhart,[50] reported 6 cases of total temporary blindness due to ethyl alcohol poisoning in which a prompt response was noted to the parenteral use of thiamine hydrochloride in doses of 10 or 50 mg. In the current year Johnson [51] added 5 cases of treatment with thiamine hydrochloride, 12 mg. daily. Four of the patients were cured. The 1 who did not respond had incipient atrophy when first seen. Laval [38] reported a similar isolated case, as did Cronin, cited by Buschke.[4] Levine reported a case of alcoholic optic neuritis [4] with classic symptoms occurring in a pellagrin. Histologically the optic nerves and chiasm showed atrophic changes.

Riboflavin has been suggested for the treatment of multiple sclerosis.[52] Goulland and Goodall-Slater obtained "interesting results" in the cases of 86 per cent of their patients so treated, but they made no mention of the effect on the nystagmus or on the optic nerves. According to Grosz,[23] the treatment is being tried in cases of tabetic atrophy of the opitc nerve.

Motor anomalies are mentioned a few times in the literature. Aside from the extraocular muscle paralyses associated with hemorrhagic superior polioencephalitis,[47] with which retinal hemorrhage is also a prominent symptom, Marchesini and Papagno noted muscular involvement in cases of beriberi,[4] and Soriano and Puiggari [41] stated that such involvement is frequent. Levine and Kyrlov independently reported diplopia associated with pellagra.[4] Grosz [23] mentioned ocular muscle paralysis and postdiphtheritic paralysis of accommodation, as well as Adie's syndrome, as possibly benefited by thiamine and riboflavin.

Special mention should be made of the conditions attributed by Wagener and Weir [46] to nutritional deficiency following persistent vomiting. They observed optic neuritis, retinal hemorrhages, paralysis of the ocular muscles and nystagmus. These symptoms are suggestive of hemorrhagic superior polioencephalitis (Wernicke's disease), in which mental symptoms are also present and which Ecker and Woltman [47] concluded is due to avitaminosis B, probably to deficiency of thiamine and of nicotinic acid. They reported marked therapeutic success in cases in which similar symptoms were present.

---

49. Carroll, F. D.: Importance of Diet in Etiology and Treatment of Tobacco-Alcohol Amblyopia, Arch. Ophth. **18**:948 (Dec.) 1937.

50. Carroll, F. D., and Goodhart, R.: Acute Alcoholic Amaurosis, Arch. Ophth. **20**:797 (Nov.) 1938.

51. Johnson, L. V.: Alcohol-Tobacco (Toxic) Amblyopia Treated with Thiamin Chloride, Arch. Ophth. **21**:602 (April) 1939.

52. Schachter-Nancy, M.: Question of Vitamin Therapy of Sclerose in Plaques, Rev. méd. de Nancy **66**:51 (Jan. 15) 1938.

Other ocular conditions noted in the presence of vitamin B deficiency or perhaps helped by vitamin B therapy are: uveitis (Lane, cited by Buschke;[4] Grosz[23]); chorioretinal disturbances allegedly due to foci of infection (Yudkin[24] [avitaminosis A also involved]); asthenopia (Lane); glaucoma and constriction of the retinal vessels (Buschke[4]), and "retinal hemorrhages with numerous white spots" (Cronin, cited by Buschke[4]).

SUMMARY

The various components of the water-soluble group of vitamins are briefly defined.

The ocular effects of avitaminosis B are fully reviewed with respect to both clinical ophthalmology and experimentation on laboratory animals.

CONCLUSIONS

1. Subclinical avitaminosis B is widespread among persons of all classes and may have unsuspected clinical manifestations.

2. Persons with ocular disease in whose cases the dietary history or the general symptoms suggest the possibility of vitamin deficiency should receive the benefit of vitamin therapy, either for a specific effect or as an adjunct to other treatment.

3. In ophthalmologic practice benefit from administration of vitamin B can be expected in cases of toxic amblyopia, retrobulbar neuritis, certain corneal conditions, Wernicke's disease and similar depletion syndromes and possibly in cases of uveitis and chorioretinal involvement of unknown cause.

4. There is ample evidence to show that administration of riboflavin will arrest cataracts in riboflavin-deficient animals, but there is no evidence that a similar effect occurs in the human being, with the possible exception of arrest of the swelling of the lens in cases of intumescent senile cataract.

5. It must be remembered that nutritional deficiencies are multiple; that thiamine relates to neuritis without degeneration; that riboflavin deficiency leads to degeneration of nerve tissue; that nicotinic acid is also involved, especially with relation to the skin and mucous membranes, cerebral symptoms and the eighth nerve; that the remainder of the complex undoubtedly plays a part in human nutrition as yet undetermined, and that other vitamins, notably vitamin A, may be implicated. Moreover, the administration of one component of the vitamin B complex tends to deplete the supply of others; so the administration of one fraction should be supplemented by the administration of the whole complex.

6. In treatment, only biologically standardized preparations should be used, with adequate doses to insure an oversupply to the patient.

The optimum requirements are five times the minimum requirements, and therapeutic doses are multiples of the optimum. Toxic effects can occur, but only from enormous doses. Although ingested, a vitamin may still not be available to the patient's physiochemical economy. The mere name of a vitamin on a label does not insure adequate therapeusis.

7. The assumption that because a lack of vitamin B causes certain symptoms in laboratory animals similar symptoms in the human being are due to deficiency of this vitamin is fallacious, illogical and not borne out by clinical experience.

8. Clinical reports by physicians should contain data to establish the premise of a deficiency and should record in detail the vitamin given, the method of administration, the dosage by weight and/or standard units and, better still, the actual product used and where it was obtained.

REPORT OF CASES

CASE 1.—*Endogenous retrobulbar neuritis.*

J. E. P., a man aged 43, employed for many years in a garage, came to my office on March 12, 1940, stating that he had had a tender left upper bicuspid for about a month. Three days previously he had noticed some blurring of the left eye. He had had the tooth extracted the day before consulting me. He volunteered that there was an area of disturbed vision involving the fixation point of the left eye. He used little tobacco and no alcohol. With his present glasses, which had been obtained under mydriasis three and a half years before, the following data were obtained:

Vision in right eye, 6/6; read Jaeger test type 1 at 14 inches (36 cm.).

Vision in left eye 6/22; read Jaeger test type 19.

Both pupils reacted to light and in accommodation, and there were no inflammatory symptoms. The right fundus was entirely normal, as was the left with the exception of definite distention of the retinal veins. In the left eye the form field was normal and the red and green fields slightly contracted. The blindspot, plotted at 75 cm., measured 75 by 80 mm., which was well within normal limits. At the same distance there was a circular relative scotoma measuring 60 by 58 mm., equally distributed around the fixation point. In this area colors were not perceived with a 0.5 degree test object but could be perceived with a 1 degree test object. The value of the colors, however, was impaired within the scotomatous area. Retrobulbar neuritis, of course, was present.

The patient was given a subcutaneous injection of 2 cc. of thiamine chloride solution, affording him a dose of approximately 30,000 units. The next day the vision had improved to 6/12 + 3 and he read Jaeger test type 6 at 15 inches (38 cm.). He was able to recognize the colors on the 0.5 degree test object at 75 cm. without impairment of the color value. The dose of thiamine was repeated.

On the following day the vision was 6/6 slowly and he read Jaeger test type 3 at 15 inches. He was still conscious of the visual disturbance, but the scotoma could not be mapped for colors with the finest test objects. Thiamine hydrochloride (30,000 international units) was again given.

On the third day after examination (fourth visit) the patient's visual acuity was 6/6 + and he could make out Jaeger test type 1 at 15 inches. Because of the

marked improvement with thiamine the dose was repeated, and serologic and sinal investigations were not made.

Similar injections were given on the sixteenth and on the eighteenth of the month. On the fifth day after he had presented himself the vision was 6/5 easily and he read Jaeger test type 1 at 15 inches. It was impossible to define any scotomatous area. The only subjective complaint was some sensation of dazzling on attempting to read. The patient is still under treatment.

Comment.—It is quite likely that the apical abscess was the cause of the retrobulbar neuritis, and it may well be argued that extraction of the tooth would have been followed by prompt amelioration. The excellent recovery of visual acuity following injections of thiamine hydrochloride, however, suggests that the inflammation of the nerve was probably due to an endogenous toxin combined with a thiamine deficiency in a manner similar to that observed in the mechanism of toxic amblyopia.

CASE 2.—*Intumescent senile cataract.*

Mrs. D. I., aged 73, had had refraction performed on many occasions. In 1936 her distance correction was:

Right eye + sph. 0.25 D. ⊃ + cyl. 62 D., axis 180
Left eye + sph. 1.50 D. ⊃ + cyl. 37 D., axis 90

At that time the lenses were clear. Six months later the distance correction for the right eye was — sph. 0.75 D. ⊃ + cyl. 1.00 D., axis 160. There was no change in the left eye. Eleven months later still more minus sphere was accepted, and on Feb. 6, 1939, the refraction was as follows:

Right eye — sph. 2.00 D. ⊃ — cyl. 2.00 D., axis 80
Left eye + sph. 0.50 D.

The value for blood sugar was well within normal limits. Because of the increased minus lens, the patient was given vitamin B complex by mouth for three months, at the end of which time there was an increase of — sph. 0.50 D. in the acceptance for distance vision in each eye. At that time a course of treatment with riboflavin was begun, the patient receiving an injection of 1 ampule (250 micrograms) of synthetic riboflavin three times a week until twenty-five injections had been given. Since that time she has taken vitamin B complex by mouth for alternate months, and in the eight months since the treatment was started there has been no further refractive evidence of swelling of the lens, no discernible increase in the lenticular opacities and no further loss of visual acuity.

Comment.—This case would tend to bear out Yudkin's suggestion that vitamin B is of value in the treatment of intumescent senile cataract. The patient noted a marked increase in her general sense of well-being, indicating a physiologic need for the vitamin.

CASE 3.—*Trachoma; corneal ulceration.*

Mr. W. M. had lost his right eye from trachoma several years previously and was under treatment for trachoma of the left eye by another physician. At the time he was referred to me he had active trachoma and a large abrasion of about one third of the corneal surface, in the lower portion. This was possibly of traumatic origin. He was hospitalized, and treatment was instituted, including administration of azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-

1'-hydroxynaphthalene-3,'6'-disulfonate) and later of sulfanilamide. The condition of the lid improved markedly, but the cornea remained soft, with various areas staining with fluorescein from day to day. Ethylmorphine hydrochloride was not employed. In three weeks the trachomatous condition of the lids disappeared, but the cornea remained refractory despite the employment of intravenous injections of typhoid vaccine, which produced satisfactory reactions and subsidence of the ciliary injection. He was given vitamins A, B, C and D, the water-soluble group being in the form of vitamin B complex sufficient to furnish 1,000 international units of thiamine daily. Two days after the vitamin treatment was started the cornea healed, and it remained healed. The patient has been observed since that time, and the conjunctiva appears absolutely normal

Comment.—The interest in this case is that the refractive corneal condition was apparently markedly benefited by the addition of vitamins to the treatment, but whether the result is to be attributed to vitamin B or to the vitamins more concerned with epithelial resistance is problematic.

CASE 4.—*Herpes of lid.*

D. B., a boy aged 13, presented himself on March 4, 1940, complaining of pain and swelling of the right upper eyelid. The lid was red and swollen, with a colony of herpetic vesicles near the outer canthus. There was also unilateral follicular conjunctivitis with mild catarrhal symptoms. There was very slight injection of the bulbar conjunctiva, which completely blanched on administration of epinephrine. There were no blebs on the cornea, and no visual disturbance was present. A mild zinc lotion was prescribed for the conjunctivitis, and thiamine hydrochloride was administered hypodermically as follows: 30,000 international units (0.1 Gm.) on the first visit, and one-half that dose for four successive days. Improvement was very rapid, and in five days the desiccated blebs were hardly discernible and the swelling practically gone.

Comment.—The antineuritic property of thiamine is evident in this case. In a second case, of severe herpes zoster involving the whole distribution of the first division of the fifth nerve, the condition failed to respond to thiamine until intravenous injections of potassium iodide were added.

CASE 5.—*Bell's palsy.*

In January 1940, Mr. E. W. C., aged 54, reported for refraction. He had a facial nerve palsy of the peripheral type on the left side. It was of ten days' duration and was attended by so much tearing that refraction was impossible. He was given a single injection of 1,100 international units of synthetic thiamine hydrochloride. As he lived out of town, I prescribed 2,000 units of thiamine hydrochloride by mouth daily for a week and then 1,000 units daily for two weeks. On returning a month later the patient stated that the facial paresis started clearing the day after the injection and that within two days he was able to whistle. At the second visit there was no evidence of facial weakness.

Comment.—The rapid improvement is probably attributable to the antineuritic properties of thiamine. Two additional patients responded similarly.

CASE 6.—*Tic douloureux.*

Miss B. D., aged 71, had typical symptoms of tic douloureux in the third division of the right fifth nerve. She had had similar attacks two years previously, which had remitted. Her attacks of pain were always controlled by injections of 15,000 to 20,000 international units of synthetic thiamine hydrochloride, the improvement being maintained for a while by administration of adequate amounts of vitamin B complex by mouth. Despite the fact that two or three large injections of thiamine hydrochloride always relieved an attack, the pain would return in ten days to two weeks, and it was necessary to inject an anesthetic into the gasserian ganglion.

Comment.—The antineuritic properties of thiamine were apparently demonstrated in this case, but without lasting benefit.

CASE 7.—*Opacities in the vitreous.*

Mrs. I. N. S., aged 73, had had a few fine opacities in the vitreous of the right eye and many fine and large opacities in that of the left eye for at least ten years. On repeated refractions the vision in the left, or more affected, eye had varied from 6/9— to 6/6—. Repeated general and special examinations had failed to reveal any significant facts. Iodides given over a long period had not produced any improvement. In 1930 a suspicious tooth was extracted and an apical abscess discovered. In 1931 another tooth was removed, with similar findings. In December 1937 the patient reported for refraction and with compound hyperopic lenses obtained in the right eye vision of 6/5 slowly and in the left eye vision of 6/6 — slowly. The slit lamp revealed no corneal changes and no lenticular opacities. The opacities in the vitreous were apparently less in each eye. There were moderate retinal arteriosclerosis and beginning senile change in the maculas. The patient was given vitamin B complex by mouth in optimum doses, which she continued intermittently for two years. The last refraction was performed in December 1939, the vision obtained being 6/5— in the right eye and 6/7.5— in the left. There was no apparent change in the opacities.

Comment.—In view of the long duration of the hyalitis prior to the institution of vitamin therapy, it is problematic whether any improvement was to be expected.

CASE 8.—*Low grade chronic uveitis.*

Mr. X. T. H., a lawyer aged 62, had had refractions performed in my office many times. On Sept. 21, 1938, he complained of sensitivity to light and considerable blinking. The diagnosis of low grade chronic uveitis was based on fine opacities in the anterior portion of the vitreous and incipient peripheral lenticular opacities which had not been present on examination a year before. The remainder of the ocular examination, including corneal microscopic study, failed to show any abnormality except a rather markedly tesselated fundus. There was no history of nasal disturbances, and the presence of sinusitis was not established. The tonsils had been removed. The Wassermann and Kahn reactions were negative. Complete blood counts revealed no abnormality. The urine was normal. General physical examination by a competent internist revealed no abnormality. Urologic consultation revealed a small amount of pus in the prostate, which cleared after three treatments. The patient was given by mouth full doses of vitamins A, C and D, with vitamin B complex from natural sources sufficient to furnish him 1,000 international units of thiamine daily. This treatment was

continued for three months, without any apparent benefit. At the end of this time other therapeutic measures were instituted.

CASE 9.—*Keratitis (traumatic?).*

Mr. V. T. B., aged 49, had an alleged mild injury to the right eye on Aug. 23, 1935. Some time subsequently an inflammatory condition developed, first in the allegedly injured eye and later in the opposite eye. It was characterized by reduced vision, marked photophobia and redness. The patient had been under the care of other physicians and was seen in consultation on Jan. 10, 1940, at which time both eyes had a marked inflammation of the palpebral and bulbar conjunctivas with some brawniness of the skin of the lids. In the right cornea there was a fan-shaped triangle of infiltration with the apex down, with vascularization, and at the apex of this area there was a small corneal ulcer. In the left eye the lower half of the cornea had a similar appearance, but there was no ulceration. There was deep-seated ciliary injection in both eyes, more marked on the left. The vision was markedly reduced. There were no deposits on Descemet's membrane; no cells were noted in the aqueous; the pupillary reactions were normal; the tension was normal in each eye, and examination of the fundi after the use of a local anesthetic showed no gross changes.

Treatment was carried on in another office. It consisted of administration of atropine sulfate and epinephrine bitartrate, applications of silver nitrate to the palpebral conjunctiva every third day, intermittent use of ethylmorphine hydrochloride, hot compresses, and 30,000 U. S. P. units daily of vitamin A.

Further examination disclosed negative Wassermann and Mantoux reactions. Cultures of material from the conjunctival sac showed a pure culture of staphylococci.

The patient was again seen in consultation on February 26, at which time there was some improvement in all the subjective and objective symptoms but the patient was far from well. Oral administration of vitamin B complex (sufficient to give 1,000 international units daily) was added to the treatment, as well as seven daily injections of riboflavin, each of 250 micrograms. These were discontinued, as no more of the substance was available. There was no improvement after two weeks.

Comment.—Although riboflavin is said to have benefited some patients with keratitis, there was no favorable response in this case. It is possible that the treatment was of insufficient duration. Marked improvement followed intravenous injections of typhoid vaccine.

CASE 10.—*Phlyctenular keratoconjunctivitis.*

Mrs. B. W. H., aged 40, presented herself on March 18, 1940, complaining of feeling a foreign body in the left eye which she thought had been present for a week. No foreign body was found, but there was a small phlyctenule at the limbus, at 9 o'clock, with a fasciculus of blood vessels leading thereto. An injection of 15,000 international units of thiamine hydrochloride was given, and a maintenance dose of vitamin B complex by mouth was prescribed. In forty-eight hours the phlyctenule had entirely disappeared.

Two additional patients exhibited in a similar rapid response, but 1, with severe involvement, failed to respond until injections of riboflavin were added.

EFFECT OF REDUCED CONTRAST ON VISUAL ACUITY AS MEASURED WITH SNELLEN TEST LETTERS

ELEK LUDVIGH, PH.D.
BOSTON

The use of Snellen test letters is the most common clinical method of determining visual acuity. Nevertheless, the effect that varying the contrast between the letters and the background produces on visual acuity, measured under modern clinical conditions, does not appear to have been investigated heretofore. This problem is of interest from several points of view. It is generally believed that high contrast is essential for the clinical testing of visual acuity. Complaints have been made [1] that the blackness of the letters and the whiteness of the card employed in the Snellen test charts vary from chart to chart and with the age of the chart. Attempts have been made to have test charts constructed in which the figures are maximally black.[2] Various questions now arise: 1. Is constant and maximal contrast important in the testing of visual acuity? 2. It has been suggested [3] that refractive errors be corrected in such a fashion that the light difference sensitivity is maximal. Will the correction thus obtained provide maximal visual acuity? 3. As will appear in a subsequent communication, it can be demonstrated that some patients with amblyopia ex anopsia have reduced light difference sense at the fovea. What effect does this reduced light difference sense have on the visual acuity? In order to supply at least tentative answers to these and other questions it is necessary to investigate the manner in

From the Howe Laboratory of Ophthalmology, Harvard University and the Massachusetts Eye and Ear Infirmary.

1. (*a*) Lebensohn, J. E.: Scientific and Practical Considerations Involved in the Near-Vision Test with Presentation of a Practical and Informative Near-Vision Chart, Am. J. Ophth. **19**:110, 1936. (*b*) Ferree, C., and Rand, G.: The Testing of Visual Acuity: I. Factors in the Sensitive Use of the Test for the Detection of Errors of Refraction, ibid. **17**:29, 1934. (*c*) Jackson, E.; Black, N. M.; Ewing, A. E.; Lancaster, W. R., and Fagin, R.: Report of Committee on Standardizing Test Cards for Visual Acuity, Tr. Sect. Ophth., A. M. A., 1915, p. 242.

2. Lancaster, W. B.: Subjective Tests for Astigmatism, Especially Astigmatic Charts, Tr. Am. Acad. Ophth. **20**:167, 1915.

3. Luckiesh, M., and Moss, F. K.: New Method of Subjective Refraction Including Identical Technics in Static and in Dynamic Tests, Arch. Ophth. **23**:941 (May) 1940.

which visual acuity as clinically measured with the Snellen test letters varies when the contrast between the letters and their background is reduced.

The apparatus employed and the procedure followed in this investigation have already been described,[4] with the exception of one feature. That feature is the test chart. Snellen test charts with reduced contrast are not available and, indeed, do not appear ever to have been commercially manufactured, although Bjerrum [5] described and employed such charts. It was therefore necessary to construct the charts. They were made by painting the letters in various shades of gray on a white cardboard background.

The various shades of gray were produced by mixing white and black "poster color" paints in varying proportions. Preliminary investigation with various mixtures approximately established the functional relation between the proportions of the two paints and the resulting reflection coefficient of the mixture. Mixtures having the desired reflection coefficients were then prepared, and the letters and a test patch were painted with each mixture. Since, in general, the letters afforded too small an area to be effectively measured by the Macbeth illuminometer, the reflection coefficients of the test patches were determined. The sources of error in these determinations of the reflection coefficients are such that it is believed that the true contrasts may be 2 or 3 per cent greater or less than their observed values. As will appear from the data, this possible error cannot affect the general nature of the conclusions. Four different degrees of contrast were employed, 5.3 per cent, 6.8 per cent, 34.4 per cent and 96.1 per cent. Contrast is defined here as the difference in brightness between the letters and the background divided by the brightness of the background. The average intensity of illumination on the chart was 23 foot candles. At the Massachusetts Eye and Ear Infirmary the Snellen charts in the vision room are illuminated by two laterally situated double light sources. The intensity of illumination on the different lines of the chart varies between 12 and 18.4 foot candles. The intensity of illumination employed in this investigation is of the same order of magnitude as the intensities provided in the usual clinical testing of visual acuity. It must be remembered, however, that the conclusions later drawn may not be valid for very high or for very low intensities of illumination.

---

4. Ludvigh, E.: Extra-Foveal Visual Acuity as Measured with Snellen Test Letters, Am. J. Ophth., to be published.

5. Bjerrum, J.: (*a*) Undersøgelser over formsans og lyssans i forskellige øjensygdomme, Copenhagen, W. Prior, 1882; (*b*) Untersuchungen über den Lichtsinn und den Raumsinn bei verschiedenen Augenkrankheiten, Arch. f. Ophth. (pt. 2) **30**:201, 1884.

Results were obtained for the right eyes of 3 observers (C. N., E. C. and E. L.) and are presented in table 1.

The values for visual acuity considerably exceed 20/20, but, as has already been pointed out,[4] this is due in part to the adoption of an arbitrary standard of visual acuity. If Snellen letters of a size corresponding to those used in obtaining the data in table 1 were presented, 60 per cent of the letters would be correctly read. The Snellen visual acuity and the refractive error of the right eyes of the 3 observers, as tested in the usual fashion, are given in table 2.

Examination of table 1 shows that for all degrees of contrast employed the individual differences between the 3 observers are less than one line on the usual Snellen test chart. The accompanying graph shows the average results for the 3 observers, the maximal visual acuity

TABLE 1.—*Results (Right Eye)*

Contrast, per Cent	Visual Acuity			
	C. N.	E. C.	E. L.	Average
96.1	20/ 9.59	20/10.18	20/ 9.90	20/ 9.89
34.4	20/11.66	20/12.54	20/12.60	20/12.27
6.8	20/18.26	20/19.77	20/18.79	20/18.94
5.3	20/25.50	20/22.50	20/29.79	20/25.76

TABLE 2.—*Visual Acuity and Refractive Error*

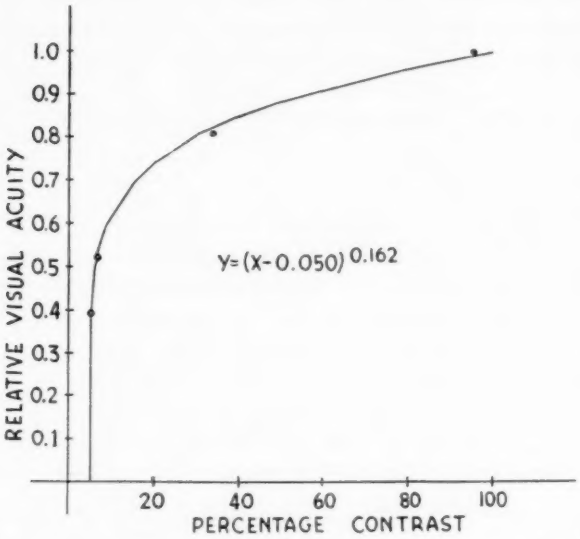
E. L.	20/15	— 2.00 D. sph. ⊃ — 1.00 D. cyl., axis 68
E. C.	20/15	— 3.62 D. sph.
C. N.	20/15	+ 0.75 D. sph. ⊃ + 0.37 D. cyl., axis 90 (not worn during the experiment)

of each observer with 96.1 per cent contrast being taken as 1 and the visual acuity with the various other degrees of contrast being expressed as a fraction in terms of the maximal acuity. The observed points are shown as circles, while the solid line is a graph of the expression $y = (x - 0.050)^{0.162}$. An examination of the chart shows that as the contrast between the letter and the background is increased from a subliminal value the visual acuity mounts very rapidly at first but more and more slowly thereafter. Thus, at low degrees of contrast visual acuity varies markedly with contrast, but at high levels of contrast relatively great changes in the degree of contrast have slight effect on the visual acuity.

One may conclude that if the test letters and the background of a Snellen chart provide reasonably high contrast (above approximately 60 per cent) the relatively slight variations attributable to differences in manufacture will have little effect on the visual acuity. Similarly, variations in contrast attributable to differences in whiteness of the back-

ground with age of the chart will have little effect on the visual acuity. A decrease in the reflection factor of the white background will, in addition to reducing contrast, bring about a reduction in the general level of intensity, but moderate variations in brightness are known [6] to have but slight effect on visual acuity.

It is possible to determine a refractive error of the eye when the highest visual acuity is not being exercised. Two methods of decreasing the acuity are reducing the intensity of illumination [7] and reducing the contrast [8] between the test object and its background. When the acuity is decreased, the size of the test object must be correspondingly increased. Thus, Luckiesh and Moss [8] reduce the contrast between the



Average results in 3 cases. Observations were taken only at the points indicated by open circles.

test object and its background until "this object when viewed with the naked eyes presents the same order of visibility as the 20/200 characters on the Snellen chart." It thus appears that when their final determination of the refractive error is made the apparent contrast between the test object and the background is very low. This means that the test is made under conditions corresponding to the low contrast and low visual acuity portion of the accompanying graph. Here visual acuity as measured by the Snellen chart is almost wholly dependent on

6. Ludvigh, E.: The Gradient of Retinal Illumination and Its Practical Significance, Am. J. Ophth. **20**:260, 1937.

7. Ferree, C. E., and Rand, G.: Intensity of Light in Relation to the Examination of the Eye, Brit. J. Ophth. **20**:331, 1936.

contrast. It therefore seems likely that a spectacle lens which produces the greatest contrast sensitivity will also produce the greatest visual acuity according to the Snellen test when the contrast between the letters and the background is low. The situation may be quite different when the contrast between the letters and the background is high. Thus, during the usual clinical testing of maximal visual acuity the conditions are such that the high contrast, high visual acuity portion of the accompanying graph is effective. Here visual acuity as measured by the Snellen test chart is relatively independent of the degree of contrast. It is therefore not a priori evident that a spectacle lens which produces the greatest contrast sensitivity will also produce the greatest visual acuity as tested by the usual Snellen test chart. Thus, it has been reported by Middleton [8] that making the boundary line between two adjacent visual fields diffuse does not affect the minimal perceptible difference in intensity between the two fields unless the region of diffusion subtends more than 5 minutes of arc at the nodal point of the eye. It seems highly probable, however, that lesser degrees of diffusion would seriously impair visual acuity. Luckiesh and Moss found that about —0.75 D. must be added to the spectacle lens indicated by the usual methods of refraction in order to achieve the maximal light difference sensitivity as determined by their method. These facts suggest that maximal contrast sensitivity is available with one adjustment of the eye, while maximal visual acuity at high contrasts requires a different adjustment. In the absence of further evidence one should not assume that the spectacle lens which produces the greatest contrast sensitivity will also produce the greatest visual acuity according to the Snellen test at high contrasts.

As has been mentioned, I have found that in cases of amblyopia ex anopsia the light difference sense at the fovea may be normal or reduced relative to the unaffected eye. It is clear that a loss of visual acuity cannot be attributed to defective light difference sensitivity when the light difference sense is normal. When, however, the light difference sense is reduced, it might be thought that the impaired light difference sensitivity accounts for the low visual acuity. The following considerations indicate that this is probably not true. It is difficult to imagine what the patient sees when employing an amblyopic eye the light difference sensitivity of which is reduced. If attention is directed to a small white disk of paper, the patient ordinarily states that the disk appears equally bright when each eye is alternately occluded. Occasionally the disk may appear brighter to the sound eye, possibly because it is more distinctly seen, but if a neutral filter eliminating only 40 per cent of the light is placed before the sound eye the disk appears brighter as viewed

8. Middleton, W.: Photometric Discrimination with a Diffuse Boundary, J. Optic. Soc. America **27**:112, 1937.

by even a highly amblyopic eye. This indicates that the apparent absolute brightness of an object as viewed by the two eyes is similar even though the light difference sensitivity of the two eyes is not the same. This condition is difficult to simulate in the normal person. The light difference sensitivity of the eye may be reduced by anoxemia,[9] but anoxemia possibly has a direct effect on visual acuity also and its effect on apparent absolute brightness is unknown. By employing a fixed background brightness and increasing the brightness of the Snellen letters, however, one may approximately simulate the condition existing in the visual mechanism of a patient with amblyopia ex anopsia and a reduced light difference sense. The apparent absolute brightness is unchanged, and a reduced physical contrast is supplied. An eye with normal light difference sensitivity and stimulated with low contrast is probably not exactly analogous to an eye with reduced light difference sense stimulated with high contrast, but no better analogy is immediately apparent. With the aforementioned reservation in mind, one can infer the loss of acuity which should be attributable to various degrees of reduction of light difference sensitivity. The contrast present between letters and background on the usual Snellen test chart is about 93 per cent, but this value, because of specular reflection, varies to a considerable extent with the angle of incidence of the light on the chart. Reference to the chart indicates that 93 per cent contrast results in the visual acuity being about 99 per cent of its maximal value. In order to reduce visual acuity to about one-half normal, or 20/40, for instance, the contrast would need to be reduced to 6 per cent, or about one fifteenth of the value of 93 per cent of the Snellen chart. By analogy and with the reservations previously mentioned, it appears that the light difference sensitivity of an amblyopic eye would need to be decreased to one fifteenth of its normal value in order to reduce the visual acuity to even 20/40. As will appear in a subsequent communication, there are few patients with amblyopia ex anopsia and central fixation in whom the light difference threshold of the amblyopic eye is fifteen times as high as that of the sound eye. One may therefore conclude that in general a decrease in the light difference sensitivity of an eye with amblyopia ex anopsia cannot account for the low visual acuity which that eye exhibits. A central scotoma, which is frequently found in patients with amblyopia ex anopsia, does not, as is commonly believed, suffice to account for the observed low acuity.

9. McFarland, R., and Evans, J.: Alterations in Dark Adaptation Under Reduced Oxygen Tensions, Am. J. Physiol. **127**:37, 1939.

A SURGICAL TREATMENT OF SPASTIC ENTROPION

ALFRED R. ROBBINS, M.D.
LOS ANGELES

Spastic entropion of the lower lid is frequently stubbornly resistant to surgical correction. The inadequacy of methods of treatment is emphasized by the multiplicity of procedures advocated for its correction, which range from the use of adhesive tape to mutilating surgical procedures on the lid. This presentation will be confined to a description of a simple surgical procedure for correcting this condition.

The term spastic entropion is used here to mean the intermittent spastic intorsion of the free border of the lower lid. This definition excludes true cicatricial entropion.

The anatomic considerations pertinent to this discussion are the location and the attachment of the lower palpebral free border portion of the orbicularis palpebrarum muscle and the location of the tarsal ligament. The temporal third of the lower lid is composed of two layers; the anterior, or cutaneous, and the posterior, or conjunctival. The anterior part is composed of skin, cilia and fibers of the orbicularis palpebrarum muscle. The posterior part is composed of the tarsus, meibomian glands and conjunctiva. The palpebral portion of the orbicularis palpebrarum muscle runs in arches over the anterior surface of both lids, covering them and uniting at the raphe palpebralis lateralis. Under this lies the ligamentum palpebrale laterale, which is attached to the border of the orbit. At the free border of the lid there are some muscle bundles which lie near the inner margin, partly in front of and partly behind the excretory ducts of the meibomian glands, which are known as the musculus ciliaris Riolani (sive subtarsalis). This portion of the lid is easily accessible for surgical treatment.

The technic of the procedure to be described is not new, nor is it original. It was advocated simultaneously in 1935 by Poulard [1] in France and by Pokhisov [2] in Russia. The methods of the two men were similar except in the steps for final closure. My execution of the operation more closely resembles the method of Pokhisov. The procedure is simple and eliminates the spastic entropion.

1. Poulard, A.: Entropion d'origine angulaire externe: Traitement chirurgical, Ann. d'ocul. **172**:97-105 (Feb.) 1935.

2. Pokhisov, N. Y.: Operation for Spastic Entropion of Lids, Sovet. vestnik oftal. **6**:131-135, 1935.

The operative procedure is as follows: The external canthal area and the outer third of the lower lid are infiltrated with a 2 per cent solution of procaine hydrochloride. The lids are put on a stretch, and an ample external canthotomy is done with straight scissors. In the second step the outer third of the lower lid is grasped by a fixation forceps or the fingers and pulled forward and upward to make the lateral attachments taut. Straight scissors are introduced downward at the margin of the canthotomy wound at the lower lid, the points entering between the conjunctiva and the skin. The muscle attachments and the fasciae are severed downward for 1 to 2 cm. until the lid feels lax. It is in the closure of the wound that my procedure differs from previous ones. The method I adopted is as follows: Two silk skin sutures are used to close the canthotomy wound. The needle passes through the skin of the upper lip and emerges, without including conjunctiva. In the lower lip it passes through conjunctiva and emerges, without including skin. The lips of the wound are approximated and the sutures tied. This results in a slight eversion of the lower lid, which after healing is rarely noticeable. This method in my hands has proved so successful that I believe it should be popularized, as it has undoubted merit.

BOECK'S SARCOID OF THE LACRIMAL GLAND

REPORT OF A CASE

J. ROSENBAUM, M.D.
MONTREAL, CANADA

Sarcoid was first described by Boeck [1] in 1899. He failed to realize then that the condition of the skin which he described, and with which his name has been associated, was merely the outward sign of a most serious systemic disease. It was not till 1914, when Schaumann [2] published his important study of what he called lymphogranuloma benignum, that all, or nearly all, of the manifestations of this ailment were linked up in a comprehensive syndrome. The disease usually occurs between the ages of 13 and 40, but its occurrence in patients both above and below these age limits has been reported. The disease is believed to be relatively benign.

REPORT OF CASE

History.—Mrs. Z. B., aged 26, a Canadian, was first seen on Jan. 12, 1939. She complained of a swelling over the outer aspects of her eyes of about six months' duration. This swelling had progressively increased and gave her a sensation of drooping of the upper eyelids. She also complained of pain around the forehead. Nine years before she had had an appendectomy. She was subject to colds and had been told she had sinal disease. Menses began at 18 years of age and had been irregular. The patient had been married five years; she had twin boys who were living and well, and she had had no miscarriages. Her father and mother, two sisters and one brother were alive and well.

Physical Examination.—The patient was quiet and well developed. There was some drooping of the upper eyelids, especially of the outer third, which was apparently caused by an enlargement of the accessory lacrimal glands. The glands appeared to be much larger than usual, not tender, lobulated and freely movable. There was no limitation in the rotation of the globes. The vision in each eye was 20/20; the fundi, the fields of vision and the intraocular tension were all normal. Examination of the abdomen revealed a scar over the area of the appendix. The heart and lungs were normal. Results of the dermatologic examination were normal.

Glandular System: There was enlargement of the glands in the neck and around the angle of the jaw. The axillary and inguinal glands were normal.

Teeth: The dental examination showed good oral hygiene and malocclusion.

Ears, Throat and Nose: The ear drums appeared normal. The tonsils were small, scarred and cryptic; debris was expressed from both. The anterior cervical glands were palpable. The larynx appeared normal.

From the Department of Ophthalmology, Royal Victoria Hospital.

1. Boeck, C.: Multiple Benign Sarcoid of the Skin, J. Cutan. Dis. **17**:543, 1899.

2. Schaumann, J.: Sur le lupus pernio, mémoire presenté a la Société française de dermatologie et syphiligraphie, November 1914.

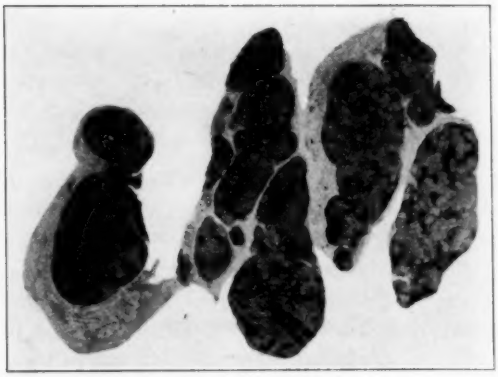


Fig. 1.—Photomicrograph of the accessory lacrimal gland; low magnification.

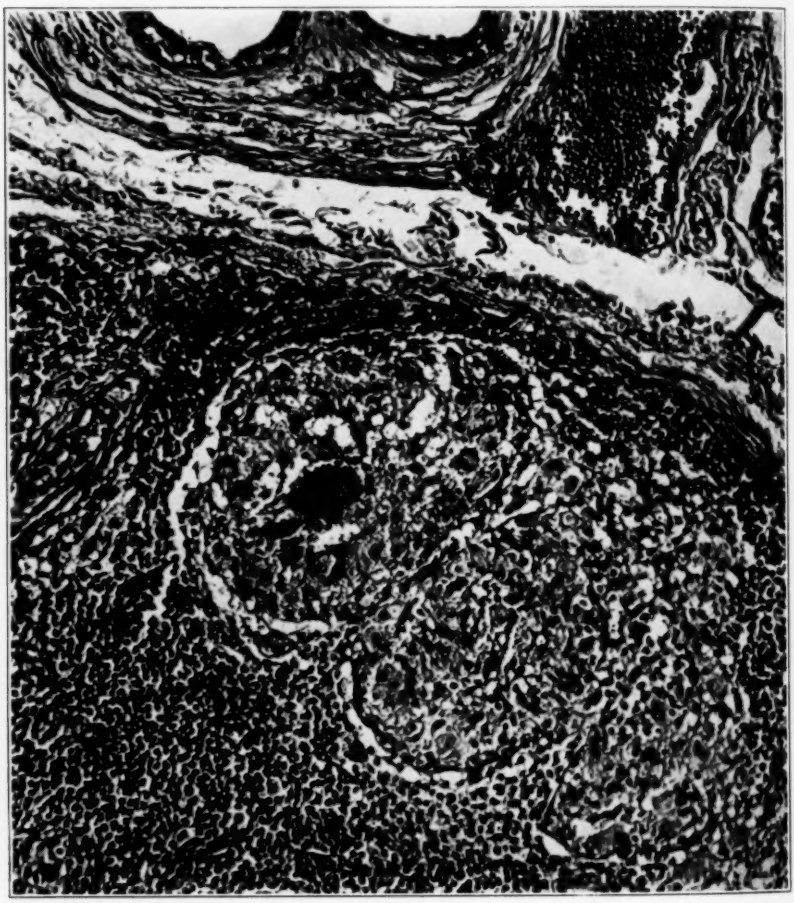


Fig. 2.—Photomicrograph of the accessory lacrimal gland, showing endothelial cells, small round cells and a few giant cells; high magnification.

The left side of the nose showed a good air passage. There were a marked septal deflection toward the right and compensatory hypertrophy of the left interior turbinate. There was no evidence of postnasal discharge. Tonsillectomy was recommended.

Laboratory Examination.—Chemical examination of the blood showed a non-protein nitrogen content of 20.2 mg. per hundred cubic centimeters, a calcium content of 10.7 mg. and normal levels of sugar and urea nitrogen. There was no anemia; the red cells numbered 5,070,000, and the hemoglobin content was 91 per cent, with a color index of 0.91. The platelet count was normal. The white cell count was normal, with a low total neutrophil count, normal eosinophil and lymphocyte counts and some monocytosis. There were some immature forms of polymophonuclear leukocytes. The sedimentation rate (22 mm. in one hour) was moderately accelerated. The Wassermann and Kahn reactions of the blood were negative, and there was a negative reaction to the Mantoux test. The urine was acid, had a specific gravity of 1.017 and showed a few epithelial cells. The basal metabolic rate was + 10 per cent.

Roentgen Examination.—The skull, feet, hands and legs showed no evidence of disease. There was no evidence of pulmonary tuberculosis; there were calcified scars in both hili.

First Biopsy.—The right lacrimal gland was excised on July 13, 1930, and a report by Dr. Waugh, of the pathology department, was as follows: The specimen consisted of an irregular, bean-sized portion of pale gray, soft tissue with a papillary surface. On section no cystic structure could be identified.

Microscopic Examination: Section showed the lacrimal gland tissue to be the seat of an extensive granulomatous inflammatory process which had led to the formation of clusters of epithelioid cells arranged in tubercles. Occasional giant cells were seen, but there were no extensive areas of coagulation necrosis.

Anatomic Diagnosis: The diagnosis was granulomatous inflammation, probably tuberculous, but because of the histologic appearance the possibility of Boeck's sarcoid could not be excluded.

Course.—The patient's tonsils were removed on July 20, and she left the hospital on July 27. She was not seen again until November 22, when she returned, complaining of enlargement of the glands in the inguinal region and in the neck. She had gained 20 pounds (9.1 Kg.) since her tonsillectomy. Examination now revealed marked enlargements of the inguinal glands on both sides, as well as of the glands in the posterior triangle of the neck on the right side. The drooping of the lid of the left eye (the eye not operated on) was hardly noticeable, and the lacrimal gland on the same side was of almost normal size.

Second Biopsy.—On November 23, a small discrete gland in the posterior part of the neck was removed for biopsy. The pathologic report was as follows: The specimen consisted of an ovoid smooth yellow gland, the size of a peanut, which on section was rather hard and yellow.

Microscopic Examination: Sections showed the lymph gland to consist of multiple small tubercle-like areas of epithelioid cells surrounded by collagenous fibrous tissue. There were occasional giant cells but little coagulation necrosis. The picture conformed to that of the so-called fibroid type of tuberculosis, which is now recognized as one of the tissue reactions found in cases of sarcoidosis.

Anatomic Diagnosis: The diagnosis was granulomatous inflammation, probably of the Boeck sarcoid type.

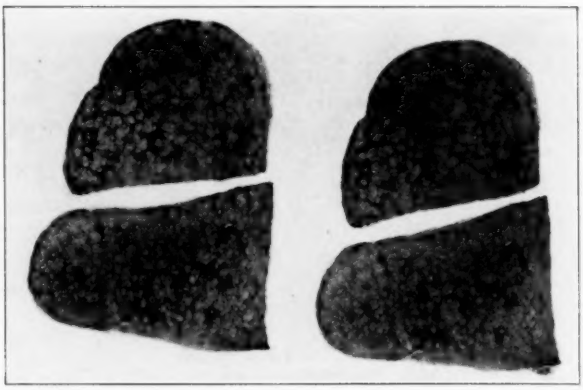


Fig. 3.—Photomicrograph of the cervical lymph gland; low magnification.

Fig. 4.—Photomicrograph of the cervical glands, showing endothelial cells, small round cells and a few giant cells; high magnification.

REVIEW OF THE LITERATURE

Relatively few cases of Boeck's sarcoid have been reported in which the ocular structures were involved. In 1917 Derby and Verhoeff [3] reported a case of sarcoid of the eyelid, as did Lehrfeld [4] in 1927. Schoeppe [5] in 1920 and Mylius [5] in 1928 reported cases of iridocyclitis. Friede [5] in 1920, Coppez [5] in 1924 and Blegvad [6] in 1931 reported cases in which there was involvement of the conjunctiva. Igersheimer [5] in 1925 reported a case in which there was involvement of the conjunctiva and the tarsus of the lower lid. In 1931 Reis and Rothfeld [7] reported a case of Darier-Roussy sarcoid of the optic nerve. Lenartowicz and Rothfeld [8] in 1930 reported cases with involvement of the brain. In 1936 Ernsting [9] reported a case of sarcoid of the eyelid with coexisting Darier-Roussy sarcoid. Palmer [10] in 1940 demonstrated that the disease can involve any part of the body. Ustvedt,[11] of Norway, recently published an account of 12 cases of Boeck's sarcoid, in 2 of which there was renal involvement and in 2 cutaneous changes. Ustvedt emphasized that pulmonary changes, especially bilateral hilar adenitis, seemed to dominate the picture in his cases. Pulmonary changes appeared in 11 of his cases and bilateral adenitis of the hilus in 9.

COMMENT

Etiology.—The etiology of the disease has not been determined. Some investigators believe it is caused by a filtrable virus. Tubercle bacilli have never been found in any of the lesions. In most instances the reaction to tuberculin was negative, as in the case reported here.

Diagnosis.—The diagnosis can be established by study of the complex manifestations in the skin, eyes, bones, glands and lungs and by

3. Derby, G., and Verhoeff, F. H.: Sarcoid of the Eyelid, Arch. Ophth. **46**:312, 1917.

4. Lehrfeld, L.: Sarcoid of Eyelids, Am. J. Ophth. **10**:255, 1927.

5. Cited by Reis and Rothfeld.[7]

6. Blegvad, O.: Boeck's Sarcoid of the Conjunctiva, Acta ophth. **9**:180, 1931.

7. Reis, W., and Rothfeld, J.: Tuberculids of the Optic Nerves as a Complication of Cutaneous Sarcoids of the Darier-Roussy Type, Arch. f. Ophth. **126**:357, 1931.

8. Lenartowicz, J., and Rothfeld, J.: Skin Sarcoid (Darier-Roussy) with Identical Changes in Brain and Internal Organs, Arch. f. Dermat. u. Syph. **161**:504, 1930.

9. Ernsting, H. C.: Boeck's Sarcoid of the Eyelid with Coexisting Darier-Roussy's Sarcoid, Arch. Ophth. **17**:493 (March) 1937.

10. Palmer, J. H.: Boeck's Disease (Sarcoid): Its Clinical Groups and Diagnosis, Canad. M. A. J. **43**:11, 1940.

11. Ustvedt, I.: Nosography and Diagnosis of Boeck's Sarcoid, Nord. med. (Norsk mag. f. lægevidensk.) **2**:1677, 1939.

biopsy. The lesions are composed of tubercles made up of nests of epithelioid and giant cells which resemble tuberculous changes, the chief point of difference being the absence of necrosis.

Prognosis.—The prognosis for life is believed to be good, although cases in which the condition ended fatally have been reported. The lesions may disappear, recur, persist or spread.

SUMMARY

A case is presented in which there was asymmetric enlargement of the lacrimal glands.

After excision of the right lacrimal gland there was a distinct diminution in the size of the corresponding gland on the left side over a period of about four months.

Within three to four months there was enlargement of the glands, of the axillary, inguinal and cervical regions.

Biopsy of a gland in the neck and a lacrimal gland showed small tubercle-like areas consisting of epithelioid cells and giant cells (no necrosis) which suggested Boeck's sarcoid.

COMBINATION OF PHOROMETER AND ACCOMMODATION RULE

ROBERT K. SIMPSON, M.D.
Lieutenant Colonel, Medical Corps, United States Army
RANDOLPH FIELD, TEXAS

In the routine physical examination of United States Air Corps personnel for flying duty the use of the multiple Maddox rod and the Risley rotary prism is an established procedure in the quantitative determination of heterophoria, in both the horizontal and the vertical meridians. Further, the rotary prism is used in estimating the abduction of the visual axes, recorded on form 64 (Adjutant General's Office) as "prism divergence." While the rotary prism is not essential in arriving at a definite conclusion as to heterophoria, it is a convenience and a time saver.

As a part of the flight surgeon's equipment there is a phorometer trial frame with an adjustable bracket and a tripod stand, a rather complex and impressive piece of equipment. Usually there is also attached a Stevens phorometer, which is rarely used. The trial frame consists of a triple cell (one rotary) for trial lenses, a Risley rotary prism and a multiple Maddox rod for each eye. There are an adjustment for interpupillary distance, a level bubble and a thumbscrew for leveling, an adjustment for a forehead rest, and on the bracket there is a "fore and aft" adjustment for tilting. On the bracket and tripod assembly there are adjustments for lateral and vertical positions. Altogether it is a rather elaborate outlay, requiring quite a bit of manipulation, the throwing out of the Maddox rod and the rotary prisms before the fixing eye and the turning and manipulating of several adjustments before the entire setup is ready for use.

In the following discussion it is to be remembered that only two instruments are actually used in the quantitative estimate of heterophoria, namely, the Risley rotary prism and the multiple Maddox rod. All other adjustments are for the sole purpose of placing these two instruments directly before the nonfixing eye. In the arrangement of the equipment used by the flight surgeon who is on a traveling flying cadet board, a great deal of space and weight is utilized by the chair clamp, the bracket and two each of the rotary prisms, Maddox rods and triple cells. Also, a great deal of time is consumed in assembling, packing and disassembling this entire unit—all for the purpose of

utilizing one rotary prism and one Maddox rod. The two of each together are never used in the examination as prescribed in Army Regulations 40-110. Two Maddox rods, that is, one before each eye, may be used clinically in the determination of cyclophoria, but an examination for cyclophoria is not prescribed for the examination of applicants for appointment as flying cadets of the United States Air Corps.

It has occurred to me that a Risley rotary prism and a multiple Maddox rod could be combined in one unit on a handle and used satisfactorily for this purpose. This is accomplished by simply removing from the phorometer trial frame the rotary prism and the Maddox rod from one side of the instrument and mounting these two on a handle. Such a unit was used on three flying cadet boards during the past year by two flight surgeons, and the results were very satisfactory. A great

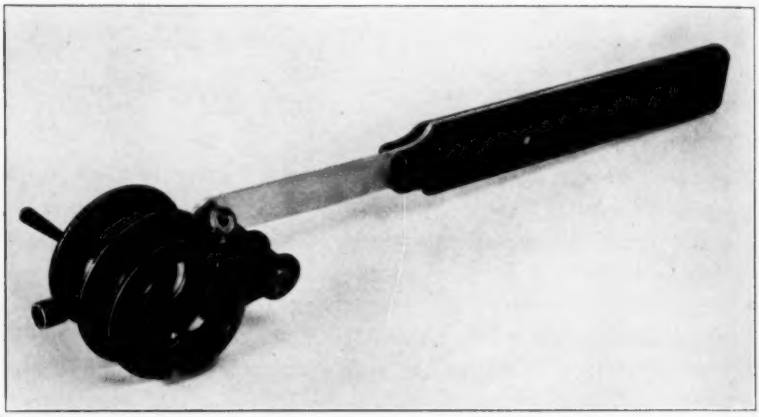


Fig. 1.—Combination phorometer and accommodation rule. (Official photograph, 2d Air Base Squadron Photo Section, G. H. Q. Air Force, United States Army, Mitchel Field, N. Y.).

deal of time was saved in the examination, and the instrument occupied less space and was easy to pack.

In using this instrument (assuming the right eye to be the fixing eye), the examinee is directed to grasp the handle with his right hand, holding the aperture of the instrument before his left eye. For the determination of heterophoria in the horizontal meridian the rotary prism is adjusted with the thumb-screw up and the Maddox rod with the axis horizontal. The examinee is then directed to locate and grasp the thumbscrew with his left thumb and forefinger. Next he is told to fix on the muscle lamp 20 feet (6 meters) away, keeping both eyes open. The eyes are screened alternately with an occluder, which assures the examiner that the "spot of light and vertical line of light" are seen

by the examinee. The examinee is cautioned to hold the handle of the instrument in the vertical position, in order that the line of light may be seen as vertical. Next he is informed that by rotating the thumbscrew about its own axis he may shift the position of the line of light toward the right or the left. He is then directed to place the line of light so that it "bisects the spot," and during this adjustment the examiner alternately screens and uncovers the nonfixing eye with an occluder. The findings are then read and recorded (base in, exophoria; base out, esophoria, etc.). Next the Maddox rod is adjusted with its axis vertical, producing a horizontal line of light, and the thumbscrew

Fig. 2.—Use of the combination instrument. (Official photograph, 2d Air Base Squadron Photo Section, G. H. Q. Air Force, United States Army, Mitchel Field, N. Y.).

of the rotary prism is rotated 90 degrees temporally. The examinee is told that the line of light is horizontal, possibly above or below the spot, and he is directed to "bisect the spot with the line" by again rotating the thumbscrew, during which adjustment the nonfixing eye is alternately screened and uncovered. The reading obtained is noted and recorded, base down before the eye indicating hyperphoria of that eye, and base up, hyperphoria of the fellow eye, etc. Next, in determining the abduction, or maximum prism divergence, of the visual axes, the examiner shifts the Maddox rod to one side, and the thumbscrew of the rotary prism is adjusted upward and slowly rotated base inward

until diplopia occurs. The reading in prism diopters is then noted and recorded.

This instrument may be much simplified, the entire assembly of rotary prism and Maddox rod being no larger than an ordinary pocket watch mounted on a handle, on one side of which may be a millimeter rule (for interpupillary distance and point of convergence on the base line) and on the opposite side the dioptric scale (up to 4 D.) and the Duane table of accommodation as to age. Thus the phorometer trial frame, bracket and tripod (or chair clamp), with the Prince rule, may be replaced by this simple compact and efficient instrument, with a great saving of time, space and weight and with facilitation of the examination. With such an instrument there may be determined: (1) heterophoria in the horizontal meridian (esophoria or exophoria); (2) hyperphoria; (3) divergence and convergence in prism diopters; (4) near point of accommodation, with ready reference to Duane's table; (5) interpupillary distance, and (6) point of convergence on the base line.

For the use of flight surgeons in the examination of applicants for appointment as flying cadets each of the two prisms composing the rotary prism may have a value of 7.5 prism diopters, giving a total maximum of 15 D. For clinical use the rotary prism may have a maximum strength of 30 prism diopters. Naturally, the 15 D. prism will be thinner and more compact.

PENTOTHAL SODIUM ANESTHESIA IN OPHTHALMOLOGY

LOUIS W. STATTI, M.D.
PITTSBURGH

Over a period of twenty-four months, anesthesia induced by pentothal sodium administered intravenously has been used with favorable results in 100 consecutive cases in which all types of ophthalmic surgical procedures were carried out on patients whose general physical conditions and ages varied widely.

All intravenously administered anesthetics were given under the direct supervision of Dr. George J. Thomas, director of the department of anesthesia of St. Francis Hospital, Pittsburgh. In this general hospital, which admits patients requiring all types of surgical procedures, this kind of anesthetic was administered in over 6,000 cases.

PREOPERATIVE MEDICATION

Good premedication is absolutely necessary for smooth pentothal sodium anesthesia. Morphine sulfate and atropine sulfate are given thirty to forty-five minutes before operation. A 0.5 per cent solution of pontocaine hydrochloride is instilled into the eye in about three doses at five minute intervals just before operation. My associates and I have found that the pontocaine hydrochloride reduces the amount of pentothal sodium which must be given, permits an earlier start of the operation and prevents the sneezing that occasionally complicates the use of intravenously administered anesthetics for surgical procedures on the eye.

INTRAVENOUS ADMINISTRATION OF PENTOTHAL SODIUM

The dose cannot be accurately determined by such factors as the patient's weight, age, sex and metabolic state. It must be adjusted to the requirements of each individual patient. To obtain the proper depth of narcosis one must resort to the technic of intermittent administration of the agent. The anesthetic is usually injected into one of the veins of the arm, ordinarily on the side opposite to the eye to be operated on. Adults are given an initial dose of 2 to 3 cc.; children and aged patients, 1 to 2 cc. The injection is then stopped to permit the appearance of the complete effect, which occurs in approximately thirty seconds. Because relaxation comes on more slowly than unconsciousness, it is important that a pause of five to ten seconds follow the injection of

From the Department of Ophthalmology, St. Francis Hospital.

each 2 to 3 cc. of the drug. Most of our patients are ready for the ophthalmic operation after the administration of 5 to 10 cc. (3 to 6 grains [0.19 to 0.38 Gm.]) of pentothal sodium. However, young adults may require a larger initial dose. If relaxation is not sufficiently advanced to permit operation, an additional 2 to 3 cc. can be injected at the same rate as in the beginning. This technic is followed throughout the operation. It must be remembered that since the agent is given intermittently the effect after the administration of each successive dose is increased. The pause between injections is highly important because the accumulated effect of the drug may come on suddenly. Evidence of recovery is an indication that an additional 1 to 2 cc. of solution is necessary. The air passage must be patent. The respirations are depressed, and for that reason it is absolutely necessary that oxygen or

TABLE 1.—*Average Dose of Pentothal Sodium and Average Duration of Anesthesia in One Hundred Cases*

Patient's Age, Years	Number of Cases	Average Dose		Average Duration of Anesthesia, Minutes
		Grains	Gm.	
4-10	5	8	0.52	21
10-20	20	18	1.16	40
20-30	10	18	1.16	33
30-40	8	15	0.97	31
40-50	12	14	0.91	23
50-60	13	14	0.91	25
60-70	17	17	1.10	26
70-80	15	12	0.78	26

a mixture of oxygen and carbon dioxide be administered continuously during the operation by means of nasal or oral adapters.

DOSES OF PENTOTHAL SODIUM USED IN ONE HUNDRED CASES

The average dose and duration of anesthesia for each age group in our series of 100 cases are given in table 1.

From our youngest patient, 4 years of age, we removed a foreign body embedded in the cornea. He was given 3 grains (0.19 Gm.) of the drug, and the anesthesia lasted five minutes. Our oldest patient, aged 78 years, underwent a modified Lagrange operation for an absolute glaucoma. He was given 10 grains (0.65 Gm.) of pentothal sodium, and the anesthesia lasted twenty minutes.

OPERATIONS PERFORMED IN ONE HUNDRED CASES

In table 2 are listed the types of operations performed in our 100 cases.

SYSTEMIC EFFECTS OF PENTOTHAL SODIUM ANESTHESIA

Only a summary of the laboratory work done in conjunction with the intravenous use of the anesthetic will be presented here. Clinical and laboratory observations are included in the paper by Dr. George J. Thomas [1] on intravenously administered anesthetics.

Blood Chemistry.—No change was observed.

Blood Count.—No change was observed.

Blood Pressure.—The drop in blood pressure varied from 4 to 40 mm., depending on the duration of the operation and the dosage of pentothal sodium used. The fall is in direct proportion to the amount of the agent administered. When a small amount of the drug was given there was no perceptible drop in pressure.

TABLE 2.—*Operations Performed in One Hundred Cases*

Type of Operation		Number of Cases
Extraction of cataract		34
Extracapsular	20	
Intracapsular	14	
Iridectomy		11
Trephining		7
Electrocoagulation for retinal detachment		3
Enucleation		11
Evisceration		1
Sclerotomy		1
Removal of foreign body with a magnet		2
Lagrange operation		1
Extirpation of lacrimal sac		3
Incision of abscess of the lid		1
Plastic operation on the globe		2
Tenotomy		2
Recession		9
Recession and advancement		9
Advancement		2
Muscle transplant		1

Pulse.—The rate varied a great deal with the individual patient. In a case of bradycardia in which the rate was 46 beats per minute, 2 cc. of metrazol was added to the initial dose of pentothal sodium solution injected. The rate increased to 72 beats per minute and remained at that level during the entire operation (time, thirty-eight minutes). The pulse returned to a rate of 46 to 50 beats per minute within two hours after the operation.

Electrocardiographic Observations.—No marked deleterious effect on the myocardium or on the conductive system of the heart was observed.

Respirations.—The respirations are extremely depressed, but, as was mentioned previously, the administration of oxygen or a combination of carbon dioxide and oxygen will increase the respiratory rate.

1. Thomas, G. J.: Clinical and Laboratory Observations in Intravenous Anesthesia, Anesth. & Analg. **17**:163-168 (May-June) 1938.

General Reaction.—Pentothal sodium can be used as often as necessary without fear of habit formation or of any deleterious mental effect. Patients are willing to submit to reoperation without fear of the anesthesia.

CONCLUSION

Experience has led my associates and me to believe that pentothal sodium intravenously administered is an ideal anesthetic for ophthalmic operations and that under the proper supervision it is easy to administer and rapid in effect. The postoperative reaction time is brief, and there are no serious complications.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

LYSOZYME AND THE ANTIBACTERIAL PROPERTIES OF TEARS

RICHARD THOMPSON, M.D.
NEW YORK

Postoperative infections of the eye were relatively infrequent even in pre-Listerian days. The earlier bacteriologists noted the comparatively few organisms which could be cultivated from the normal conjunctivas. They found that organisms placed in the conjunctival sac rapidly disappeared therefrom (Stort;[1] Bernheim;[2] Bach;[3] Hirota,[4] and others). Considerable evidence was gathered in support of the view that mechanical factors, such as constant flushing by the tears and winking of the eyelids, were responsible for keeping the conjunctivas free from organisms (Leber;[5] Stort;[1] Bernheim;[2] Bach;[3] Römer;[6] Hirota;[4] Schirmer[7]). That the tears or conjunctival fluids have a bactericidal or inhibitory action was also early suggested, and many workers attempted to demonstrate such actions in vitro.

THE ANTIBACTERIAL ACTION OF TEARS

"Tears" as usually obtained from the conjunctivas are mixtures of lacrimal and conjunctival secretions containing exfoliated epithelial cells, occasional leukocytes and probably some meibomian secretion. They can normally be obtained only in minute quantities. According to Schirmer,[7] 0.5 to 0.75 Gm. is secreted in sixteen waking hours. To obtain sufficient quantities for study it is necessary to resort to some irritation or stimulation to increase the flow. Many workers have utilized tears from eyes with epiphora resulting from conjunctival or corneal pathologic conditions. The relative proportions of the various constituents of tears are, necessarily, changed by inflammation, so that tears so obtained are not normal. For the sake of brevity, however, all such

1. van Genderen Stort, A. G. H.: Arch. f. Hyg. **13**:395, 1891.
2. Bernheim, J.: Beitr. z. Augenh. **8**:61, 1893.
3. Bach, L.: Arch. f. Ophth. **40**:130, 1894.
4. Hirota, K.: Centralbl. f. Bakt. **31**:225, 1902.
5. Leber, cited by Bernheim.[2]
6. Römer: Ztschr. f. Hyg. u. Infektionskr. **32**:285, 1894.
7. Schirmer, O.: Arch. f. Ophth. **56**:197, 1903.

TABLE 1.—*Summary of Literature on Bactericidal or Inhibiting Action of Tears*

Author	Year	Animal Species	Method of Stimulation	Normal or Pathologic	Concentration of Tears	Bacteria Tested	Results	Notes
Bernheim [2]	1893	Man	Breathing NH_3 vapor	Normal	Loop culture in 0.5-1 cc. tears	Staph. aureus B. subtilis	Marked reduction in numbers	Only with small inoculums
		Man	None	Conjunctivitis Keratitis	.....	B. prodigiosus	No effect	
Marthen [8]	1893	Man	None	Conjunctivitis Keratitis	Loop culture in 1 cc. tears	Staph. aureus	Killed in 2 hours	Loop culture in saline solution showed growth
Bach [3]	1894	Man	?	Normal	Undiluted ?	Staph. aureus B. typhosus	Killed	Saline solution had same effect
		Man	None	Conjunctivitis Keratitis Dacryocystitis	.....	Sarcinae; B. prodigiosus	No effect	
Ahlström [9]	1895	Man	None	From fistula of lacrimal gland	Undiluted ?	Staphylococcus	Slight inhibition	Considered effect merely that of unfavorable medium
				Phlyctenular disease	Undiluted ?	Staphylococcus	Slight inhibition	
de Bono, F. P., and Frisco, B.: Arch. di ottal. **7**: 195, 1899	1899	Goat Ass Calf	?	?	?	Staph. aureus; B. typhosus; V. cholerae	Decrease for 1-4 hours, then increase	
						Tubercle bacillus	Virulence lessened	
Helleberg [10]	1901	Man	None	Various pathologic conditions with epiphora	0.25 cc. tears plus 2-10 drops broth	Staph. pyogenes	Killing in 18 hours	Only with small inoculums; saline solution plus 2-10 drops broth showed growth
Zur Nedden [19]	1907	Man	?	?	75% tears	B. typhosus; B. dysenteriae; diplobacillus	All grew	

Lindahl [11]	1908	Man	Mechanical by sound in lacrimal duct	Normal ?	1 drop culture in 0.5 cc. tears	Pneumococcus; hemolytic streptococcus; staphylococcus	Diminution in numbers	Growth in saline solution controls
Schneider [20]	1910	Man	Collected by absorbent material in fornix	Normal	1 part culture; 10 parts tears	B. typhosus	No effect	
		Rabbit	Collected by absorbent material in fornix	Normal	1 part culture; 10 parts tears	B. typhosus; Staph. aureus; Streptococcus; diphtheria bacillus; xerosis bacillus; diplobacillus; meningococcus	No effect	
						Pneumococcus	Slight inhibition	
Meissner [12]	1912	Dog	Collected by absorbent material in fornix	Normal	75% tears	Cholera vibriones; dysentery bacilli; typhoid bacilli	No effect	
						Staphylococcus	Slight inhibition	
Fleming [17]	1922	Man	?	?	1% tears	Fecal streptococci; saprophytic cocci	Killing Marked killing	(Lysozyme)
Ridley [14]	1928	Man	Lemon juice	Normal	90-25% tears; 10% serum or peptone added	Staph. aureus; hemolytic streptococci; fecal streptococci; V. cholerae	Inhibition	Saline solution plus 10% serum or peptone showed growth
						B. coli; B. typhosus	No effect	
Thompson and Gallardo [15]	1940	Man	Onion vapor	Normal	50% + broth	Staph. aureus; Staph. albus	Inhibition usually complete	50% broth and saline solution; no inhibition
					25% + broth	Staph. aureus Staph. albus	No inhibition Often inhibition	

secretions may be referred to as "tears" with the provision that the conditions governing secretion and the manner of collecting be stated. Up to 1922 all workers used essentially the same technic for determining the antibacterial action of tears. Varying inoculums of the organisms to be tested were made into small volumes of diluted or undiluted tears, and constant amounts of the mixtures were plated out at intervals during incubation. By comparison of the numbers of colonies at the initial plating with those at later periods, killing, inhibition or growth of the organism was determined. The results obtained by the various workers, summarized in table 1, are contradictory, but careful analysis brings out certain facts. Staphylococci, usually aureus strains, were the organisms most frequently tested. Bernheim,[2] Marthen,[8] Bach,[3] Ahlström,[9] Helleberg,[10] Lindahl [11] and Meissner [12] all found that these organisms were killed or inhibited in various degrees by tears, although their explanations for these actions differed. Bach [3] obtained with saline solutions effects equal to those obtained with tears, and Ahlström [9] also considered the inhibiting effect to be merely that of poor nutrition. However, Marthen,[8] Helleberg [10] and Lindahl [11] added small amounts of broth to the tears and controlled their experiments with saline solution containing the same amounts of broth. They obtained growth in the saline solution but not in the tears. Bernheim [2] and also Helleberg [10] stressed the importance of the number of organisms inoculated; with too large an inoculum the antibacterial effect was masked. The preponderance of evidence collected by the early workers indicated that tears have an antibacterial action against staphylococci. The evidence regarding other organisms is less definite, because fewer tests were made with them. There was some indication that the enteric gram-negative organisms are less affected by tears. Axenfeld,[13] reviewing the subject in 1907, minimized the importance of any antibacterial action of tears but somewhat grudgingly admitted that Staphylococcus aureus appeared to be affected by them. He stated that Blair and Ogawa, working in his laboratory, could find no bactericidal action of tears against pneumococci or gonococci, but he gave no details of the methods used.

Since the discovery of lysozyme in 1922 a few studies of the antibacterial action of tears have been made by the method employed

8. Marthen: Beitr. z. Augenh. **12**:1, 1893.

9. Ahlström, G.: Centralbl. f. Augenh. **19**:193, 1895.

10. Helleberg: Mitt. a. d. Augenklin. d. carolin. med.-chir. Inst. zu Stockholm **3**:41-539, 1901.

11. Lindahl, C.: Mitt. a. d. Augenklin. d. carolin. med.-chir. Inst. zu Stockholm **9**:11 and 57, 1908.

12. Meissner, W.: Ztschr. f. Hyg. u. Infektionskr. **72**:213, 1912.

13. Axenfeld, T.: The Bacteriology of the Eye, New York, William Wood & Company, 1908, p. 77.

by the workers just mentioned. Ridley,[14] in 1928, studied tears obtained by irritating the conjunctiva with a small drop of lemon juice. He inoculated dilutions of bacterial suspensions into tubes containing various concentrations of tears with 10 per cent serum or peptone added to supply nourishment. The tests were adequately controlled with corresponding saline mixtures. Aureus staphylococci, hemolytic streptococci, fecal streptococci, pneumococci and cholera vibrios were markedly inhibited by the tears. Colon and typhoid bacilli were not affected. Ridley showed that a slight decrease in tear concentration would cause complete loss of the antibacterial action. Seventy-five per cent concentration allowed the growth of pneumococci which were killed by tears in 90 per cent concentration. Gallardo and I,[15] using pooled tears obtained by stimulation with onion vapor, inoculated dilutions of staphylococcic suspensions into various tear dilutions added to equal parts of broth. Saline broth controls were inoculated at the same time. All of the 25 coagulase-negative white staphylococcic strains were completely inhibited by tear dilutions of 1:2 and 1:4. Sixteen coagulase-positive orange strains were not inhibited by 1:4 dilutions of tears but were inhibited by 1:2 dilutions. The results in these experiments were clearly defined. Lack of nutrition could have played no part, since growth always occurred in the equivalent broth-saline mixtures. Fleming,[16] by a somewhat different method, showed that Staph. aureus is inhibited by human tears. He inoculated the staphylococci into mixtures of tears with hydrocele fluid or with serum. The mixtures were incubated in Wright slide cells; chambers were made by placing strips of filter paper treated with petrolatum between two microscope slides and, after filling with the fluid, sealing the edges with paraffin. After incubation the colonies in each mixture could be seen and counted. Tears mixed with serum or hydrocele fluid always showed markedly fewer colonies than serum and hydrocele fluid without tears.

Fleming[17] in 1922 showed that tears, in common with many other agents, have a remarkable lytic activity against many saprophytes. In view of this it was natural that tests should be made of the ability of tears to dissolve parasitic and pathogenic organisms. Fleming[17] found that some staphylococci, some hemolytic and other streptococci and some abortus bacilli were dissolved by tears diluted up to 100 times. Pneumococci and influenza, diphtheria and plague bacilli were not lysed. Malta fever organisms were not dissolved. Failure to show microscopic solution did not, of course, prove that the organisms were not affected.

14. Ridley, F.: Proc. Roy. Soc. Med. **21**:1495, 1928.
15. Thompson, R., and Gallardo, E.: Am. J. Ophth., to be published.
16. Fleming, A.: Proc. Roy. Soc. Med. **26**:71, 1932.
17. Fleming, A.: Proc. Roy. Soc., London, s.B **93**:306, 1922.

Salvatore and Rindello,[18] reported that some staphylococci, hemolytic streptococci and xerosis bacilli were dissolved by tears. Thompson and Gallardo,[15] found that four of eight coagulase-positive staphylococcic strains showed slight evidence of lysis; four strains showed no trace of solution. Of thirteen coagulase-negative strains, only one showed no lysis and seven showed more marked degrees of solution than did any of the positive strains.

In view of the recent work, which strengthens the indications of earlier reports, there can be little question that tears possess antagonistic properties against staphylococci. The work of Ridley[14] indicates also that other parasitic and pathogenic organisms are affected by tears, and, logically, there would seem to be no reason for supposing that the tears have a specific action against staphylococci.

ANTIBACTERIAL ACTION OF CONJUNCTIVAL FLUIDS FOLLOWING THE USE OF SILVER NITRATE AND OF OTHER ASTRINGENTS

Zur Nedden[19] found that, while "normal" tears had no action against typhoid bacilli, dysentery bacilli or diplobacilli, the fluids obtained from the conjunctivas after treatment with silver nitrate had a marked bactericidal action against these organisms. This action was proportional to the degree of inflammation produced by the treatment. His results were confirmed in essence by Schneider[20] in human and rabbit eyes and by Meissner,[12] in the eyes of dogs. These workers obtained the secretions by means of wads of absorbent material left in the lower fornix for about twenty minutes at various intervals after the silver nitrate treatments. The methods of testing for antibacterial action were the same as those described for the normal tears. The authors demonstrated definite bactericidal action against a variety of organisms, including typhoid bacilli, dysentery bacilli, cholera vibrios, streptococci, pneumococci, staphylococci, diphtheria bacilli, xerosis bacilli and meningococci. The actions were much more marked than those of normal tears. Schneider's[20] work indicated that the antibacterial agent in the secretions produced by the silver nitrate came from the leukocytes and was of the same nature as the antibacterial enzymes of these cells. Meissner[12] considered the possibility that traces of silver protein combination remaining deposited in the conjunctival folds accounted for the antibacterial action, since the effect gradually diminished after the first half-hour. While this was possibly the case, it does not seem probable, since all three authors irrigated thoroughly with saline solution after the silver nitrate treatment and some effect still remained after twenty-four

18. Salvatore and Rindello: Boll. d'ocul. **15**:1214, 1936.
19. Zur Nedden, M.: Ztschr. f. Augenh. **18**:301 and 315, 1907.
20. Schneider, R.: Arch. f. Ophth. **73**:223, 1910.

hours. Schneider [20] also controlled his experiments by treating with silver chloride, which had no effect. In addition, zinc sulfate, which of itself has little antibacterial action, had a definite effect in increasing the bactericidal action of the conjunctival secretions. All three workers found that the agent in the secretion resisted a temperature of 60 C. for one-half to one hour. This was, of course, compatible with the possibility that remnants of silver were responsible but was equally compatible with the concept that the responsible agent was leukocytic enzyme. On the available evidence it seems likely that these workers did increase the antibacterial effects of the conjunctival fluids by the attraction of leukocytes and the diffusion of the enzymes from these. Such experiments should certainly be repeated and elaborated.

LYSOZYME

Fleming,[17] in 1922, showed that tears, among other biologic secretions and fluids, had the remarkable property of dissolving certain saprophytic cocci rapidly and completely. He obtained evidence that the agent, or agents, concerned in this lysis was an enzyme, and he gave it the name "lysozyme," or lytic enzyme. In addition to tears, nasal mucus, sputum, various tissue extracts, vegetable juices and egg white possessed the lytic property. The ready availability of hens' eggs, which contained the lytic material in high concentrations, provided a convenient source for the large amounts of material necessary for chemical studies and made possible relatively exact knowledge of the chemical nature and mode of action of the egg white agent. As a result, the egg white agent is generally regarded as a typical lysozyme, and there can be no question that a concept of lysozyme can properly be built on the knowledge regarding it.

The Agent in Egg White Lytic for Saprophytic Micrococci.—The combined work of a number of investigators [21] has shown that the active agent in egg white which dissolves the susceptible air cocci is a basic protein or polypeptide enzyme containing about 16 per cent nitrogen and 2 to 3 per cent sulfur. It is of small molecular size, having a diameter of less than 30 millimicrons.[22] It is soluble, heat stable and filtrable in acidified aqueous mediums but is insoluble and heat labile in alkaline solutions. It is inactivated by oxidizing agents and by some heavy metals.

21. (*a*) Wolff, L. K.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **49-50:** 88, 1926-1927. (*b*) Meyer, K.; Thompson, R.; Palmer, J., and Khorazo, D.: J. Biol. Chem. **113:**303, 1926. (*c*) Roberts, E. A. H.: Quart. J. Exper. Physiol. **27:** 89, 1937. (*d*) Roberts, E. A. H.; Maegraith, B. G., and Florey, H. W.: ibid. **27:** 381, 1938. (*e*) Abraham, E. P., and Robinson, R.: Nature, London **140:**24, 1937. (*f*) Abraham, E. P.: Biochem. J. **33:**622, 1939.

22. Gildemeister, E.: Zentralbl. f. Bakt. (Abt. 1) **136:**408, 1936.

Under some conditions the inactivation is reversed by sulfide or by cyanide, making it probable that one active group contains a sulfhydryl radical.

The action of the egg white enzyme on the susceptible saprophytic cocci may be demonstrated in several ways. Most dramatic is the rapid clearing of heavy opaque suspensions of the organisms on the addition of dilutions of the agent. Microscopic examination of the cocci being acted on by the lysozyme has shown that marked swelling of the bacterial cells takes place before lysis occurs,[23] but Boasson [24] has indicated that this is only an apparent enlargement of the cells due to flattening as a result of an increase in permeability of the cell walls with passage outward of soluble cellular contents. There is general agreement that the enzyme acts on some constituent of the cell wall.

Lysozyme preparations which dissolve the air cocci also kill them or inhibit their growth. Cleared suspensions of cocci are usually sterilized. Inhibition of growth may easily be demonstrated by placing drops of lysozyme dilutions on agar pour plates containing heavy inoculums of the susceptible organisms. After incubation, wide colony-free zones in the areas of the drops show the inhibition of growth and indicate that the enzyme diffuses readily through the agar. During lysis the lysozyme is first adsorbed on the susceptible cells [25] but is freed again on their solution and may be recovered in toto from the fluid.[26] When large numbers of cells are dissolved there is probably some inhibition of the enzyme by the products of the reaction.

The chemical nature of the action of the enzyme on the bacterial membrane has been, to some extent, clarified. Hallauer [23b] suggested that it acts on a mucoid constituent. Meyer and his co-workers [27] were the first to present evidence as to the nature of the reaction. They found that a marked increase in reducing sugars was produced by the agent acting on the susceptible organisms or on certain mucoid substrates obtained from these. It was indicated that the enzyme has a specific action on the sugar linkages of certain aminocarbohydrates. This conclusion was confirmed and extended by Epstein and Chain,[28] who isolated from the susceptible cocci a nondialyzable carbohydrate sub-

23. (*a*) Kigasawa, T.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:155, 1927-1928. (*b*) Hallauer, C.: Zentralbl. f. Bakt. (Abt. 1) **114**:519, 1929. (*c*) Fleming.[17]

24. Boasson, E. H.: J. Immunol. **34**:281, 1938.

25. Fleming.[17] Boasson.[24]

26. (*a*) Fleming, A., and Allison, V. D.: Proc. Roy. Soc., London, s.B **94**:142, 1923. (*b*) Nakamura, O.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **38**: 425, 1923-1924. (*c*) Boasson.[24]

27. Meyer, K.; Palmer, J. W.; Thompson, R., and Khorazo, D.: J. Biol. Chem. **113**:479, 1936.

28. Epstein, L. A., and Chain, E.: To be published.

strate which when acted on by purified lysozyme released dialyzable materials consisting of N-acetylhexosamine and other reducing groups.

The action of lysozyme is influenced by a number of environmental factors. The rate of lysis increases with increasing temperature up to a maximum of about 60 C.[29] The hydrogen ion concentration probably determines the maximum, since it determines at what point destruction of the enzyme by heat begins. The hydrogen ion concentration also has a direct influence on lysis. The optimum p_H for lysis has been given usually as somewhere between 6 and 7.4 (Fleming;[17] Hallauer;[23b] Boasson,[24] and others), but this varies with the solubility of the bacterial proteins, which differs with different organisms.[29b] The actual optimum hydrogen ion concentration for the action of the enzyme on the carbohydrate substrate is much more acid, being about 4.[27] Lysis of susceptible organisms does not take place in distilled water because of the insolubility of the cell contents in this medium.[25] Small (0.5 per cent) salt concentrations favor lysis [20] by increasing the solubility, but higher concentrations (8 per cent) inhibit the action by preventing the absorption of the enzyme to the cell surfaces.[24]

Changes in the bacterial cells themselves also affect the action of lysozyme. Heat-killed, phenol-killed or formaldehyde-killed bacteria are not completely dissolved,[31] because of the insolubility of the changed proteins and not because of any lack of lysozyme action.[32] The medium on which the organisms are grown influences their susceptibility to some extent.[33] Fleming and Allison [26a] and Hallauer,[23b] by growing many generations of the susceptible organisms on mediums containing subactive lysozyme concentrations, produced strains which were much more resistent to the enzyme than were the original cultures.

Other Sources of Agents Which Dissolve the Saprophytic Micrococci.—Since Fleming's original work a fairly complete survey has been made of the distribution of agents able to lyse the lysozyme sensitive saprophytic cocci.[34] Practically all mammalian tissues and fluids

29. (*a*) Andersen, O.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **70**: 90, 1931. (*b*) Thompson, R.: Unpublished data. (*c*) Fleming.[17]

30. Fleming, A., and Allison, V. D.: Brit. J. Exper. Path. **3**:252, 1922.

31. Goldsworthy, N. E., and Florey, H.: Brit. J. Exper. Path. **11**:192, 1930. Gohar, M. A.: Zentralbl. f. Bakt. (Abt. 1) **119**:240, 1930. Fleming and Allison.[30] Thompson.[29b]

32. Fleming and Allison.[30] Thompson.[29b]

33. Kopeloff, N.; Harris, M. M., and McGinn, B.: Am. J. M. Sc. **184**:632, 1932.

34. (*a*) Fleming, A.: Proc. Roy. Soc. Med. **26**:71, 1932. (*b*) Florey, H.: Brit. J. Exper. Path. **11**:251, 1930. (*c*) Suranyi, L.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **49**:166, 1926. (*d*) Jermoljewa, A. W., and Bujanowskaja, I. S.: Zentralbl. f. Bakt. (Abt. 1) **122**:267, 1931. (*e*) Ridley.[14] (*f*) Roberts and others.[21d] (*g*) Anderson.[29a] (*h*) Fleming and Allison.[30]

have been found to contain agents capable of lysing the organisms. Notable exceptions are cerebrospinal fluid, normal urine [17] and normal aqueous humor.[35] The enzyme concentrations vary in the different tissues and in the same tissues in different animals. Human tears are particularly rich in lysozyme; dogs' tears contain considerable quantities, but the tears of rabbits and cats contain very little. That the lacrimal glands actually are the source of the enzyme in the tears is indicated by the facts that the dog's lacrimal gland tissue contains the agent in much higher concentration than does the mucosa,[36] and human tear gland tissue also contains a high concentration.[29b] Saliva, nasal secretions and gastric and intestinal mucus in most species contain considerable concentrations of enzyme. The spleen, kidney, liver, lung, lymph glands and intestinal and gastric mucosa have relatively large amounts. The milk of most species [37] contains lysozyme, but commercial cow's milk contains little. All pathologic exudates and transudates which have been tested dissolve the susceptible cocci. Leukocytes are especially active, containing approximately the same enzyme concentrations as human tears.[14] Eggs of birds of species other than the hen contain lysozyme in lower cnocentrations than hens' eggs. The enzyme is present in some fish eggs but apparently not in frogs' eggs. Turnips, cabbages and cauliflowers contain small amounts of the enzyme, and some bacteria have been shown to contain it.[38]

The available evidence indicates that the agents from these various sources are essentially similar to the egg white enzyme.[39] Roberts, Maegraith and Florey [21d] made careful comparisons of the agent in egg white and that in cat's saliva and found that both were basic and had similar solubility and sedimentation constants. The two agents were, however, antigenically distinct. Epstein and Chain [28] found that several agents from various sources acted in the same way on the carbohydrate substrate from the micrococci. The resistant organisms produced by Fleming and Allison [40] by the growth of sensitive strains on mediums containing various lysozymes were equally resistant to all agents regardless of the sources of the material on which they were grown. It is probable that the lytic agents from widely different

35. Cavca, V., and Prica, M.: Arch. f. Ophth. **121**:740, 1929.

36. Thompson, R., and Gallardo, E.: Am. J. Ophth. **19**:684, 1936.

37. Bordet, J., and Bordet, M.: Compt. rend. Soc. de biol. **179**:1109, 1924. Blatt, M. L., and Kessler, H.: Human Milk: Its Lysozyme Content and Bacterial Count, Am. J. Dis. Child. **53**:768 (March) 1937. Prickett, P. S.; Miller, N. J., and McDonald, F. G.: J. Bact. **25**:61, 1933. Sadakata, K.: Experimental Studies on Lysozyme, Am. J. Dis. Child. **45**:1360 (June) 1933.

38. Fleming.[34a] Meyer and others.[27]

39. Roberts and others.[21d] Fleming.[34a] Meyers and others.[27]

40. Fleming, A., and Allison, V. D.: Brit. J. Exper. Path. **8**:214, 1927; footnote *26a*.

sources are similar in chemical constitution and properties and act in an identical manner on a specific carbohydrate substrate in the susceptible cocci. Differences in chemical make-up sufficient to produce antigenic differentiation do not negate the essential identity of these enzymes.

Factors Affecting the Concentration of Lysozyme in the Secretions and Tissues.—Ridley [14] first demonstrated that hypersecretion caused an eventual diminution in the concentration of lysozyme in secretions. He showed that tears of persons who had suffered from epiphora, from whatever cause, for some time had definitely lower lysozyme concentration than did normal tears. This has been confirmed by several authors.[41] Stimulation of secretion with pilocarpine diminished the lysozyme content of dogs' tears, according to Hallauer.[41a] Atropine did not affect that of normal human tears, although it did increase the concentrations in the tears of patients with epiphora by diminishing secretion.[42] Pilcocarpine stimulation of salivary secretion in cats temporarily increased the lysozyme concentration of the saliva but eventually caused a marked decrease.[21d] Sullivan and Manville [43] found that pilocarpine stimulation exhausted the content of lysozyme in the colonic mucosa of rabbits.

The first suggestion that vitamin A intake affects lysozyme secretion was in the work of Findlay,[44] who treated xerophthalmic eyes of rats deficient in vitamin A with human tears and obtained marked improvement. Andersen [45] studied human twins suffering from xerophthalmia and found the tear lysozyme content to be much lower than normal. On the addition of vitamin A to the diet the xerophthalmia improved and the lysozyme became normal. Paradoxically, tissue concentrations of lysozyme appear to be increased in the presence of vitamin A deficiency.[46] Sullivan and Manville [43] explained this by an inability of the glands to secrete mucus. Assuming that lysozyme is secreted with the mucus as a vehicle, the enzyme is stored up in the tissues when failure to secrete mucus occurs. They ascribed this failure to a disturbance in uronic acid metabolism and supported their views by showing that menthol poisoning brought about the same train of events and that the feeding of pectin tended to overcome the disturbance.

---

41 (*a*) Hallauer, C.: Arch. f. Augenh. **103**:198, 1930. (*b*) James, W. M.: Am. J. Ophth. **18**:1109, 1935. (*c*) Thompson and Gallardo.[36]

42. James.[41b] Ridley.[14]

43. Sullivan, N. P., and Manville, I. A.: Am. J. Pub. Health **27**:1108, 1937.

44. Findlay, G. M.: Brit. J. Exper. Path. **6**:16, 1925.

45. Andersen, O.: Acta pædiat. **14**:81, 1932.

46. Prickett, P. S.; Miller, N. J., and McDonald, F. G.: J. Bact. **32**:27, 1937. Sullivan and Manville.[43]

Neither immunization with the lysozyme-sensitive cocci [47] nor injections of nonspecific protein [41b] increased the lysozyme concentrations of tissues or secretions.

The Action of Lysozyme-Containing Materials on Organisms Other Than the Sensitive Micrococci.—Saprophytes: The knowledge of lysozyme so far summarized was gained by work with the saprophytic micrococci. Most workers used the original micrococcus of Fleming, called by him Micrococcus lysodeikticus; others used various strains of sarcinae isolated from the air. It is known that many other saprophytes (bacilli as well as cocci, gram-negative as well as gram-positive) are readily dissolved by the materials which lyse the micrococci. The evidence available, while by no means conclusive, indicates that all these organisms are dissolved by the same enzyme acting in the same way on identical or similar carbohydrate substrates. The lytic action of various lysozyme-containing materials against many susceptible saprophytes of various types was consistently parallel.[29b] An agent with a high degree of activity against one organism had a high activity against all. An agent with slight activity against one was proportionately inactive against all. The work of Bordet [48] indicating that different agents had more or less specific actions against different saprophytes possibly could be explained by her failure to control the hydrogen ion concentrations during the tests. I [29b] have found that organisms differ markedly with respect to the p_H favoring solution after lysozyme action. Two agents with moderate differences in hydrogen ion concentrations could appear to act specifically on separate organisms if the solution of these organisms was favored by the respective hydrogen ion concentrations, even if the actions of the enzyme were exactly the same on both organisms.

Stronger evidence for the unity of lysozyme action against saprophytes is found in the work of Epstein and Chain.[28] From several different susceptible organisms, including gram-positive and gram-negative rods, these workers obtained carbohydrate substrates which were acted on by purified egg white lysozyme with the release of N-acetylhexosamine and other reducing substances, just as occurred with the M. lysodeikticus substrate.

Parasites and Pathogens: The general assumption has been that lysozyme attacks only saprophytic bacteria. Fleming,[34a] Ridley [14] and others, however, have maintained that some pathogenic organisms are affected by it. These authors have presented evidence that lysozyme-containing materials kill or inhibit certain parasitic and pathogenic bacteria. They apparently assumed that lysozyme must necessarily be the

47. Allison, V. D.: Brit. J. Exper. Path. **5**:165, 1924.
48. Bordet, M.: Compt. rend. Soc. de biol. **19**:1252, 1928.

agent responsible for the action. Applied to such complex materials as saliva, tears and nasal secretions, such an assumption is obviously unsound. It has been shown to be incorrect in regard to at least one secretion, saliva. This secretion has a slight but definite bactericidal and inhibiting action against diphtheria bacilli,[49] lactobacilli [50] and a number of other organisms.[51] The agent or agents acting against the first two organisms and against at least some of the others differ from lysozyme in important respects. They are heat labile in acid solutions and can be destroyed by temperatures which leave the lysozyme unchanged.[52] The lysozyme of saliva in acid preparations passes Berkefeld filters, but the lytic agents effective against diphtheria bacilli and lactobacilli do not.[20b] By Berkefeld filtration of saliva at the normal p_H Bibby [50] obtained the lactobacillus agent without the lysozyme. If confirmed, this would rule out the possibility that lysozyme plays a part in the action against this organism as an activating or activable agent cooperating with another agent.

Egg white, nasal secretions, serum and milk all [53] have some action against a number of parasitic and pathogenic bacteria and viruses. Partially purified lysozyme from egg white was shown by Wolff [54] to affect a number of pathogenic organisms, but there is some question whether or not other agents could have survived in his preparations. Indirect and inconclusive evidence [55] has indicated that the action of nasal secretions against some viruses is not due to lysozyme. The part played by lysozyme in the actions of milk and of serum is still very

49. Dold, H., and Weigmann, F.: Ztschr. f. Hyg. u. Infektionskr. **116**:158, 1934. Dold, H.: Zentralbl. f. Bakt. (Abt. 1) **135**:69, 1935. Weigmann, F., and Koehn, A.: Ztschr. f. Hyg. u. Infektionskr. **118**:507, 1936. Dold, H.; Lachele, W., and Du Dscheng Hsing: ibid. **118**:369, 1936. Weigmann, F., and Noeske, H.: ibid. **119**:413, 1937. Casassa, M. T.: Gior. di batteriol. e immunol. **18**:381, 1937; abstracted, Bull. Hyg. **12**:524, 1937.

50. (*a*) Clough, O. W.: J. Dent. Research **14**:164, 1934. (*b*) Hine, M. K.: ibid. **15**:305, 1935. (*c*) Taylor, W. E., and Bibby, B. A.: ibid. **15**:178, 1935. (*d*) Bibby, B. G.: ibid. **16**:325, 1937; (*e*) **17**:308, 1938. (*f*) Clough, O. W.; Bibby, B. G., and Berry, G. P.: ibid. **17**:493, 1938. (*g*) Bibby, B. G.; Clough, O. W., and Hine, M. K.: J. Am. Dent. A. **25**:1290, 1938. (*h*) Hill, T. J.: ibid. **26**: 239, 1939.

51. Grabner, A.: Ztschr. f. Stomatol. **32**:987 and 996, 1934. Pesch, K. L., and Damm, R.: Ztschr. f. Hyg. u. Infektionskr. **118**:1, 1936. Prica, M.: ibid. **119**: 306, 1937. Berg, A.: ibid. **120**:450, 1938.

52. Taylor and Bibby.[50c] Thompson.[29b]

53. For references see Thompson, R.: Lysozyme and Its Relation to the Antibacterial Properties of Various Tissues and Secretions, Arch. Path. **30**:1096 (Nov.) 1940.

54. Wolff, L. K.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:188, 1927.

55. Burnet, F. M.; Lush, P., and Jackson, H. V.: Brit. J. Exper. Path. **20**: 377, 1939. Francis, T.: Science **91**:198, 1940.

obscure. From leukocytes of various species extracts have been obtained which killed or inhibited a number of pathogenic bacteria.[53] The properties of the active agents (behavior with precipitating agents and solubility and heat stability in acid solutions) suggest that they closely resemble lysozyme and are probably similar basic proteins. There is at present no evidence to indicate whether or not they are identical with the lysozyme of the leukocytes and produce the same chemical changes on the same substrate or whether additional enzymes with different activities are involved.

Lysozyme of Tears.—Measurements of Concentrations: Fleming[17] estimated the concentrations of lysozyme in various materials by determining the greatest dilution of the agent which would produce an arbitrary degree of lysis of a standard suspension of the susceptible organisms. This method has been used by most workers who have reported on the concentration of lysozyme in the tears in different pathologic conditions or after various treatments. It is subject to the errors involved in all serial dilution methods, and it is uncertain to what extent the wide variations in lysozyme titers of supposedly normal tears found by those workers[56] who tested a sufficient number of normal persons were due to the errors of the method or to actual differences in concentrations. An improvement in the method of titration would be desirable. Boasson[24] used a method for determining the difference in density of the bacterial suspensions caused by lysozyme which involved the measurement of light absorption thermoelectrically. With repeated tests on the same material his errors were always less than 5 per cent and Gallardo and I[15] used the photoneflectometer of Libby, which measures turbidity photoelectrically, and found it to have about the same degree of accuracy. The test organisms, however, varied unpredictably in sensitivity from time to time, so that it is not possible to compare accurately the lysozyme concentrations of tears tested at different times. It remains to be seen whether organisms dried or otherwise preserved will keep a constant sensitivity over a long period and thus enable accurate quantitative comparisons of tears tested at different times to be made. It may be that a chemical method of titration by measuring the activity of tears on the pure carbohydrate substrate can be devised.

Factors Affecting Tear Lysozyme: The effects of vitamin A deficiencies and of several drugs on the lysozyme concentrations of tears have been discussed in the general discussion of lysozyme. The relation of various pathologic conditions to tear lysozyme has also been mentioned but deserves a somewhat more extended discussion. Several of the papers on the relation are not individually very convincing, in view of the difficulties in measurement already discussed and because of the

56. Thompson and Gallardo.[36] James.[41b]

authors' failure to test a sufficient number of normal samples. The general agreement of all workers on most points, however, suggests that the conclusions may nevertheless be valid.

Ridley [14] measured the lysozyme concentrations in tears by determining the greatest dilutions which when mixed with agar would inhibit the growth of a sensitive gram-positive bacillus isolated by him. He did not give the number of normal samples tested or the range of variation in these but merely stated that his pathologic samples had a certain percentage of the "normal" lysozyme activity.

All other workers have determined the highest dilutions of tears which would produce an arbitrary amount of clearing of a standard suspension of the sensitive micrococci. Hallauer [41a] and also Cavca and Prica [35] each used only 10 normal samples to establish their normal variations. James [41b] and also Gallardo and I [36] tested respectively 100 and 72 normal samples. It is significant that these workers found a much greater degree of overlapping of the pathologic with the normal. In spite of the difficulties and deficiencies there was general agreement as to the tendency for the tear lysozyme concentration to decrease, especially in the presence of acute conjunctivitis or of a corneal pathologic condition resulting in severe epiphora. In the presence of chronic conjunctivitis the diminution was usually less marked. In cases of trachoma the titer was related to the stage of the disease; in the acute stage and with corneal involvement the titers were low but tended to approach normal in the chronic stages (also Mourzinn and Souchkowa [57]). There was no relation between lysozyme titer and age, sex or race.

Antiseptics and Lysozyme.—The possibility that tear lysozyme may play a part in the natural defense against infection has led a number of workers to investigate the effect on it of a number of antiseptics. Other things being equal, an antiseptic which had little injurious effect on lysozyme would be more desirable than one which was injurious. In their investigation on the chemical nature of lysozyme Meyer and his associates [21b] showed that it was susceptible to iodine and heavy metal cations. Ridley [58] studied a number of antiseptics commonly used in ophthalmologic practice as to their bactericidal power in comparison with their effect on lysozyme. Copper sulfate, silver nitrate, acriflavine, mild protein silver and mercury oxycyanide were all injurious to lysozyme. Zinc sulfate, mercury perchloride, mercury biniodine, phenol and boric acid had little effect on it. He, however, found that the persistency of the antibacterial action of silver nitrate,

57. Mourzinn, A. N., and Souchkowa, E. G.: Rev. internat. du trachome **12**:1, 1935.

58. Ridley, F.: Proc. Roy. Soc. Med. **25**:480, 1932.

remaining as silver chloride, outweighed its injurious effect against lysozyme, especially since it was still actively bactericidal in dilutions which had no action on lysozyme.

James [41b] found that zinc sulfate injured lysozyme in the concentration used by him, as also did optochin and metaphen. Some of the problems and difficulties involved in the in vitro assessment of antiseptics when such factors as lysozyme are taken into account are illustrated by my work in collaboration with Isaacs and Khorazo.[59] We determined the bactericidal actions against staphylococci of the highest usable concentrations, that is, of the highest concentrations

TABLE 2.—*Antiseptics Studied in Relation to Bactericidal Effect and Injury to Lysozyme*
(Adapted from Thompson, Isaacs and Khorazo [59])

Antiseptic	Usable Concentration,* Percentage	Percentage Staphylococci Killed in 1 Minute by Usable Concentration	Percentage of Bactericidal Action Remaining After 50% Dilution of Antiseptic	Highest Concentration Percentage Causing no Injury to Lysozyme	Percentage of Usable Concentration Which Injured Lysozyme
Merthiolate	0.1	15.3	100	0.02	620
Gentian violet	0.01	54	25	0.0002	62
Phenylmercuric nitrate	0.01	66	90	0.0012	12
Zephiran (a mixture of alkyldimethylbenzyl ammonium chlorides)	0.04	99.9	50	0.004	10
Acriflavine	0.05	80	50	0.004	8
Iodine	0.025	99	25	0.0005	2
Chlorazene	0.1	40	25	0.001	1
Mercurochrome	2.0	33	25	0.002	0.1
Mild protein silver (argyrol)	25.0	45	100	0.024	0.1

* Highest concentration causing no severe irritation of rabbits' conjunctiva by standard method.

which caused no marked irritation of a rabbit's conjunctiva when applied by a standardized method. We determined also the effect of dilution on this bactericidal action and then the highest concentration which caused no injury to lysozyme. Our results are summarized in table 2.

All the substances tested injured lysozyme if sufficient concentrations were used. Except in the case of merthiolate the concentrations necessary to affect lysozyme were definitely less than the usable concentrations, in some cases very much less. In assessing from such work the possible value of an antiseptic it is, of course, a matter of personal judgment what weight should be given to each property—how much, for instance, an unfavorable effect on lysozyme should

59. Thompson, R.; Isaacs, M. L., and Khorazo, D.: Am. J. Ophth. **20**:1087, 1937.

weigh against a marked bactericidal effect or against an action which holds up well with dilution. This work, however, illustrates the various factors which probably determine the clinical value of antiseptics, and such studies ought to be useful in the preliminary assessment of such values.

The indirect action of antiseptics on lysozyme has not been adequately studied. Cavca and Prica,[35] in a very limited series, tested tears taken fifteen to thirty minutes after various antiseptic drops had been used. They reported that collargol (colloidal silver and silver oxide) and targesin (a diacetyl–tannic acid–silver preparation) caused a marked drop in lysozyme secretion but that boric acid and zinc sulfate had no effect. Hallauer[41a] found that lysozyme titers lowered as a result of infection were increased by zinc or yellow ointment treatments which improved the clinical condition.

The Part of Lysozyme in the General Antibacterial Action of Tears.—Fleming[17] and also Ridley[14] assumed that all the antibacterial actions of tears were due to lysozyme. Since tears contain such high lysozyme concentrations, there is some justification for this assumption, but the obviously complex constitution of tears makes it an unsafe one. The outstanding property of lysozyme, its resistance to heat in acid solutions, offered a possibility of ruling out this agent in any antibacterial action which could be destroyed under these conditions. Helleberg[10] and Ridley[14] both found that the antibacterial actions of tears were destroyed by boiling, but neither controlled the p_H during the heating. Gallardo and I[15] boiled acidified tears for five minutes, neutralized them and compared the inhibiting action of these against orange and white staphylococci with the action of fresh unboiled tears. The unheated tears inhibited both types, as has been described, while the boiled tears had lost all activity against the staphylococci, although their lysozyme content was entirely unchanged. These experiments were repeatable, and the results were clearly defined, leaving no doubt that lysozyme alone is not responsible for the action of tears against staphylococci. They did not rule out the possibility that the tear lysozyme may act in conjunction with some other factor, heat labile in acid solutions,

The probable role of leukocytic enzymes in the increase of the bactericidal action of conjunctival fluids by silver nitrate and other astringents suggests that an antibacterial agent in normal tears may originate from the leukocytes. Such agents obtained directly from leukocytes have been shown, like lysozyme, to be themostable in acid solutions; so such an origin would not account for the heat-labile factors. The exact nature of the antibacterial action of tears against various organisms and the part played in them by the lysozyme secreted by the tear glands are still to be clarified.

THE ROLE OF THE ANTIBACTERIAL ACTIONS OF TEARS IN THE DEFENSE OF THE EYE SURFACES

In spite of the prevailing ignorance of the exact mechanism concerned, there is no doubt that tears have an antibacterial action against saprophytes and against some pathogens. The possible role of these actions in the defense of the eye against infections deserves some discussion. It is obvious that the extremely lysozyme-sensitive saprophytes cannot become parasitic or pathogenic on the ocular membranes as long as these membranes are bathed in tears with such a marked action against them. A first step in the successful evolution from susceptible saprophyte to parasite would certainly require the development of a mechanism of resistance to the lysozyme, whether or not this were the only requirement for such a step.

It is more difficult to determine whether the tears play a role in the resistance to parasitic and pathogenic organisms on which they act only in high concentrations. Ridley [14] expressed the opinion that the antagonistic action of tears is of great importance in preventing infection. He found that staphylococci obtained from patients with keratitis and conjunctivitis on first isolation readily infected rabbits' eyes but in cultures lost virulence rapidly. The same organisms, preserved in the infected eyes over the same period retained their original virulence. Ridley ascribed this preservation of virulence to the antibacterial action of the tears and indicted that it was the lysozyme which was responsible by showing that the organisms grown on agar containing egg white also retained their virulence. Since in vitro inhibition occurred only with concentrated tears, Ridley expressed the belief that a slight drop in lysozyme concentration would enable infection of the eye to take place. He presented some evidence that such a drop in lysozyme concentration is likely to lead to infection. A patient with chronic dacryocystitis had acute conjunctivitis and a hypopyon ulcer when the tear lysozyme was diminished as a result of long-continued epiphora caused by a foreign body. There are obviously other possible explanations for this and other similar findings published by Ridley, but they are, at least, compatible with the view that the lysozyme concentration was the controlling factor.

The relation between vitamin A intake and lysozyme adds interest to a recent report on a relation between the vitamin A content of the blood and the severity of gonorrheal ophthalmia in adults. Sei-Boen-Lian,[60] in a study of 84 patients, found that the group of 41 with severe corneal involvement had significantly lower blood levels than the group of 19 with no corneal involvement. Patients with slight corneal involvement had intermediate blood levels. If vitamin A should

60. Sie-Boen-Lian: Ophthalmologica **99**:496, 1940.

be conclusively shown to affect the severity of gonococcic infection of the eyes it would not necessarily follow that it did so through the medium of changing lysozyme concentrations, but the possibility is interesting.

The role of the antibacterial agents of tears, lysozyme or others, in the defense of the eye is still obscure, and much further work will be required to clarify it. The problem is of sufficient interest and possibly of sufficient practical importance to make research on it of value to ophthalmologists.

TREATMENT OF OCULAR INFECTIONS WITH LYSOZYME (EGG WHITE)

Among the various remedies for the eye used in prescientific medicine, egg white held a prominent place. In James's "History of Ophthalmology" [61] there are repeated references to the use of the whites of eggs, beginning in the earliest Roman and Anglo-Saxon periods. At this late date one has no way of knowing whether egg white was more or less efficacious than the less frequently recommended "urine of a virgin" or "rain water caught on Ascension Day," but the discovery of lysozyme adds interest to its use in folk medicine. Ridley,[14] in 1928, advocated that egg white be given a trial in cases of infection of the eyes. The only reports of its actual use of which I am aware are those of Melnik and Natanson.[62] These authors reported favorable results in the treatment of blepharitis, conjunctivitis, dacryocystitis and keratitis. The most convicting report is that on the treatment of 42 patients with blepharitis of one to ten years' duration. These had all previously been treated by "all known methods" without permanent or durable relief. Thirty-two of them were improved "far beyond previous results." Three were completely cured. The authors stressed that their patients had not been followed for a long period. Their report is suggestive but far from conclusive. Attempted repetition with egg white and with concentrated lysozyme preparations would seem desirable. It would also be interesting to determine whether leukocytic enzymes have any effect on such conditions, since these apparently have more action against pathogens than does egg white.

---

61. James, R. R.: History of Ophthalmology to 1800, London, Cambridge University Press, 1933.

62. Melnik, M., and Nathanson, P.: Bull. Inst. Metchnikoff **3**:133, 1936.

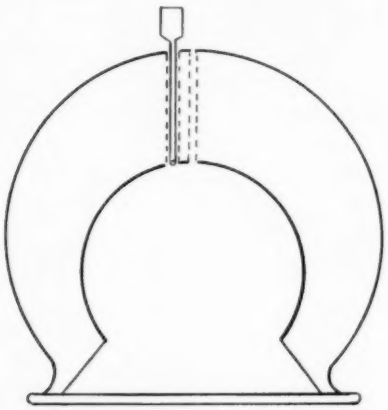
Clinical Notes

AN IMPROVEMENT IN THE GONIOSCOPE CONTACT GLASS TO FACILITATE FILLING WITH FLUID

BENJAMIN FRIEDMAN, M.D., NEW YORK

The use of the contact lens for gonioscopy is often attended with considerable difficulty in expelling the air bubble from the hollow of the glass. The maneuver of lifting the rim causes discomfort to the patient, and there is a tendency for the liquid to flow over the face and nose. The surface of the glass becomes soiled by the operator's fingers.

To be able to fill the contact glass with fluid while the glass remains in position over the patient's eye would be a distinct advantage. To this end I caused a narrow channel to be drilled through the center of the glass and another about 2 mm. away; both these holes communicate with the cavity of the glass, which is above the cornea. A hypodermic needle



Method of filling contact glass through needle. Egress of air takes place through other channel.

of proper bore which has been shortened to correspond with the thickness of the glass and blunted is introduced into the eccentric hole, and the contact glass is placed on the eye. A small 2 cc. syringe is filled with saline solution and connected with the adapter of the needle. The fluid is then gently forced into the cavity of the contact glass; the air escapes from the central hole as the fluid enters and allows complete filling with comparative ease. The butt of the needle in situ offers a convenient handle for manipulating the contact glass.

Lenses of plastic materials lend themselves more readily to drilling than those of glass. The channels do not interfere with the useful visibility of the lens, as the central parts are not ordinarily employed for observation.

I venture to suggest that this apparatus could be employed for the study of chemical interchange between the cornea and solutions introduced into the cavity of the contact glass.

The lens was made for me at the Obrig Laboratories, 7 East Forty-Eighth Street, New York.

Correspondence

CONJUNCTIVITIS IN ERYTHEMA EXUDATIVUM MULTIFORME

To the Editor:—It was with great interest that I read the article by Dr. Martin P. Koke on Conjunctivitis in Erythema Exudativum Multiforme in the January issue of the ARCHIVES (**25:** 78, 1941). I am glad that Dr. Koke classified under this title the cases reported by Dr. Wheeler and by Dr. Bailey and also by Drs. Stevens and Johnson. There is no question that all these do belong in the group which Dr. Koke has so well described.

At Mount Sinai Hospital I have observed 3 cases of this condition in the past two years, and I felt that the immediate administration of sulfanilamide was able to prevent any ocular complications other than mild irritation of the conjunctival vessels. Whether this drug is really of any use in such cases could, of course, be determined only if all patients with the condition were so treated.

J. LAVAL, M.D., New York.

SERRATED DISCISSION KNIVES

To the Editor:—I accept in an appropriate spirit Dr. Parker's generous congratulations (ARCH. OPHTH. **25:** 156 [Jan.] 1941) on the excellence of my serrated discission knife. It is true that my knife is different from his in that, judging from his own statements, it is far more efficient, but it is identical with his in principle in that it is a serrated Ziegler knife. I share his amazement that my knife should have "stood up" for twenty years in spite of frequent use, but I largely attribute its longevity to its freedom from abuse and to the fact that it has been sterilized only in alcohol. I cannot understand why he should wonder "what and where these serrations are," for they are plainly shown in the illustration.

The purpose of my letter was simply to point out that a serrated discission knife of remarkable efficiency and durability had once been constructed and to suggest that attempts should be made to duplicate it. This matter is not unimportant; a discission knife sometimes converts practically complete blindness into useful or even normal vision. It is interesting to learn from Dr. Parker's letter that "Boston capsules" are tough while "Philadelphia capsules" are tender. From the tone of his letter, I surmise that also certain Philadelphia *digiti pedum* are tender.

F. H. VERHOEFF, M.D., BOSTON.

News and Notes

EDITED BY W. L. BENEDICT

SOCIETY NEWS

Association for Research in Ophthalmology.—The twelfth scientific meeting of the Association for Research in Ophthalmology will be held on Tuesday, June 3, 1941, at 9:30 a. m. in the Empire Room of the Hotel Cleveland in Cleveland. The program has been prepared as follows:

"Studies in Capsular Permeability and Lens Swelling," John G. Bellows, M.D., Department of Ophthalmology, Northwestern University Medical School, Chicago.

"The Relation of Epinephrine to the Secretion of the Intraocular Fluid," J. S. Friedenwald, M.D. and W. Buschke, M.D., Johns Hopkins University and Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital, Baltimore.

"Multiple Extraocular Muscle Transplants in Monkeys," P. J. Leinfelder, M.D., Department of Ophthalmology, State University of Iowa, Iowa City.

"The Protein Content of the Aqueous Humor in Man," Peter C. Kronfeld, M.D., Department of Ophthalmology, Illinois Eye and Ear Infirmary, Chicago.

"The Spectral Sensitivities of the Color Receptors as Measured by Dark Adaptation," Joseph Mandelbaum, M.D., and Esther U. Mintz, Ph.D., Department of Ophthalmology, Bellevue Hospital and Biophysics Laboratory, Columbia University, New York.

"Physiologic Studies on Neural Mechanisms of Visual Localization and Discrimination," Charles C. Talbot, M.D., Department of Ophthalmology, Johns Hopkins Hospital, Baltimore.

"Experimental Contributions to the Problem of Vitreous Detachment," L. von Sallmann, M.D., Department of Ophthalmology of the College of Physicians and Surgeons, Columbia University, New York.

"Gliomas of the Retina: Histogenesis and Histopathologic Classification," Edith M. Parkhill, M.D., and W. L. Benedict, M.D., Department of Pathology and Department of Ophthalmology, Mayo Clinic, Rochester, Minn.

Pan-American Medical Association.—The Eighth Congress of the Pan-American Medical Association, which was to have been held in Buenos Aires, Argentina, in August 1941, has been postponed until 1942. The exact date will be determined and announced later.

UNIVERSITY NEWS

Appointment of Dr. Charles A. Bahn.—Dr. Charles A. Bahn has been appointed professor of ophthalmology at the Louisiana State University School of Medicine at New Orleans. Dr. Theodore J. Dimitry is professor of ophthalmology and director of the department.

FOREIGN NEWS

Ophthalmological Society of Egypt.—The annual congress of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, on Friday and Saturday, March 14 and 15, 1941, at 9 a. m. The symposium for the congress will be on (1) blepharitis (Soliman lecture) and (2) glaucoma.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

DEFECTIVE CLOSURE OF THE NEURAL TUBE: A CASE OF INVOLVEMENT OF THE CENTRAL OLFACTORY, TRIGEMINAL MESENCEPHALIC, VISUAL REFLEX, AUDITORY AND CEREBELLAR SYSTEMS. H. S. RUBINSTEIN and W. FREEMAN, Arch. Neurol. & Psychiat. **44:** 636 (Sept.) 1940.

With regard to the visual system, the comment is as follows:

The presence of bilaterally light reflexes in the presence of rather marked hypoplasia of the right superior colliculus is interesting. On the basis of earlier reports which postulated the flow of constrictopupillary impulses from the optic tract to the superior colliculus, one was led to believe that damage to one superior colliculus would abolish the light reflex or at least lead to unilateral pupillary changes. Later observations on cats and monkeys have shown that afferent light impulses destined for pupillary constriction traverse the optic tracts along the medial margin of the lateral geniculate body to enter the brachium of the superior colliculus, through which they are transmitted to the neuraxis.

The neuraxial level in which they terminate is not the superior colliculus but the thalamomesencephalic junction (pretectal area). After synapse in the pretectal area, secondary fibers take two courses: (1) through the posterior commissure to end in the Edinger-Westphal nucleus of the contralateral side and (2) distoventromedially to terminate in the Edinger-Westphal nucleus of the ipsilateral side. That all fibers destined for the contralateral Edinger-Westphal nucleus do not cross through the posterior commissure may be gathered from the fact that midline section of the posterior commissure reduces but does not abolish the consensual light reflex. While this observation was made on the cat, it probably also holds for higher mammals, since in apes the crossing fibers in the posterior commissure are probably less numerous than in the cat.

It is obvious from this that a defect in the neural tube which involves one superior colliculus and even the posterior commissure can still spare the light reflex. In this case the lesion did not extend to the pretectal region, nor did it involve the medial border of the lateral geniculate body. Some of the commissural fibers must have been involved, however, since the pupillary light reflexes were sluggish bilaterally.

R. IRVINE.

Color Sense

A NEW SUBJECTIVE COLOR MANIFESTATION. J. SEGAL, Compt. rend. Soc. de biol. **133:** 259, 1940.

Segal suggests that color sensation depends on the frequency of the nervous impulses acting on the retinal elements. This is indicated experimentally by revolving a disk of black cardboard carrying a white

sector of 90 degrees. In varying the speed and illumination, the image becomes dominated in turn by red, green and blue in brilliant saturation. This phenomenon is cortical, as it is seen by myopes equally well with or without glasses.

J. E. LEBENSOHN.

Conjunctiva

TUBERCULOSIS OF THE CONJUNCTIVA. W. H. MCKENZIE, Am. J. Ophth. **22:** 744 (July) 1939.

McKenzie gives Bordley's classification of tuberculosis of the conjunctiva and discusses the various types. He reports a case of the disease in an 18 year old Negress, whose right upper lid was drooping, thickened and swollen, particularly in its outer third. The adjoining palpebral conjunctiva was thickened, red and studded with raised granulomatous papules about 1.5 mm. in diameter. The right lower lid was similarly involved, but here the process was more extensive. General physical examination gave negative results, but the tuberculin test gave a markedly positive reaction. A biopsy specimen was taken, and tissue was excised for guinea pig inoculation. Both tests gave positive results. Roentgen treatment appeared efficacious.

W. S. REESE.

OCULOGLANDULAR DISEASES WITH SPECIAL REFERENCE TO TULAREMIA AND PARINAUD'S CONJUNCTIVITIS. V. R. HURST, Am. J. Ophth. **22:** 891 (Aug.) 1939.

This is Hurst's second report, of 4 cases, making a total of 23 cases of oculoglandular disease observed by the author. He gives the following summary.

"In 23 cases of oculoglandular disease, with histologic studies on 12, no clinical difference was noted between cases in which the leptothrix was found and cases in which it could not be demonstrated. Two cases of oculoglandular tularemia were sharply differentiated from the cases of Parinaud's conjunctivitis by their clinical course and agglutination reaction, which bears out the contention that these are separate disease entities."

W. S. REESE.

Congenital Anomalies

CONGENITAL PREPAPILLARY CYST CONTAINING A MOVING VASCULAR LOOP. J. M. LEVITT and R. I. LLOYD, Am. J. Ophth. **22:** 760 (July) 1939.

The case of a 15 year old girl is reported. She was told by the school physician that there was something wrong with the left eye. Each eye had vision of 20/40. Under homatropine cycloplegia vision of 20/40 was improved to 20/20 with a —0.50 sphere. The media and fundus of the right eye were normal. The media of the left eye were clear. There was a grayish white circular elevation covering part of the disk and extending beyond it at the lower inner margin. With the Gullstrand binocular ophthalmoscope this was found to be a cyst, and a loop was seen within, moving up and down behind the retinal blood

vessels with every motion of the eye. The blind spot was moderately enlarged, and with red-free light the binocular scope showed the nerve fibers running across the front of the cyst. The peripheral field of the eye was about 10 degrees less than its fellow. W. S. REESE.

PERSISTENT PUPILLARY MEMBRANE WITH UVEAL ECTROPION, HYPERPLASIA OF THE STROMA AND ATYPICAL IRIS COLOBOMA. J. B. HERTAULT and JOSE SVEDLICK, Arch. de oftal. de Buenos Aires **24:** 651 (Aug.) 1939.

A case is reported of a dense pupillary membrane occupying the external two thirds of the pupillary space. This is contrary to the rule. The membrane sprang from the margin of the pupil. The internal circumference of the pupil presented an ectropion of uveal pigment. Beside a general rarefaction of the iris stroma with marked hyperplasia of the anterior layers of the iris, there was a horizontal Y-shaped iris coloboma largely occupied by the remains of the pupillary membrane, the horizontal arm being formed by a string of tissue, probably a remnant of fetal tissue.

The present status of this lesion is reviewed. A classification of the different varieties is given, and the development and etiopathology of these anomalies is discussed. C. E. FINLAY.

Cornea and Sclera

HISTOLOGIC AND ETIOPATHOGENETIC ASPECTS OF DEGENERATIVE CORNEAL PANNUS. M. CORRADO, Ann. di ottal. e clin. ocul. **67:** 881 (Dec.) 1939.

After a review of the literature, the author reports histologic observations in 12 eyes. Ten were enucleated for secondary glaucoma resulting from uveitis, trauma, cataract extraction and other causes. The other 2 were the exciting eyes in cases of sympathetic ophthalmitis with hypotony. The following conclusions were drawn: The pannus consists chiefly of infiltrating cells from the vessels at the limbus, which pass beneath the corneal epithelium, followed by new vessels. The cells become converted to connective tissue, which raises the epithelium from Bowman's membrane. Cells from the corneal stroma also find their way through defects of Bowman's membrane to a location beneath the epithelium. In a few cases, when a wound has penetrated the cornea cells and vessels from the iris grow between Bowman's membrane and the epithelium. Whenever the epithelium is raised from Bowman's membrane, tissue from the limbus tends to grow over this membrane.

The article is accompanied with photomicrographs and a bibliography.

S. R. GIFFORD.

LATTICE-LIKE CORNEAL DYSTROPHY. E. HESSE, Arch. f. Ophth. **141:** 1, 1939.

The pedigree of an Austrian family is reported, 8 members of which (belonging to three generations) were suffering from the lattice-like form of corneal dystrophy. The inheritance was of the dominant type.

The very early stages of the disease could be studied in several cases. In these early stages the slit lamp revealed three types of changes: (1) fine dendritic irregularities in Bowman's membrane or just behind it, located in the center of the cornea; (2) polygonal or star-shaped opacities in the same location and (3) peripheral arcuate opacities which may have been due to ruptures of Bowman's membrane.

P. C. KRONFELD.

CLINICAL AND HISTOLOGIC OBSERVATIONS IN A CASE OF PRIMARY POSTERIOR TUBERCULOSIS OF THE SCLERA. S. SUGANUMA, Klin. Monatsbl. f. Augenh. **103:** 208 (Aug.) 1939.

A student aged 22 had suffered from exudative pleurisy for six months prior to the onset of episcleritis in the temporal equatorial area of his left eye. Pirquet's reaction was strongly positive. Exophthalmos, detachment of the retina and papillitis were noted. Histologic examination showed an intrascleral tumor measuring 12 by 8 mm. in cross section. It contained numerous typical tubercles, and there were pathologic changes in the retina and the choroid. The author stresses the fact that primary choroidal tuberculosis did not exist in this case.

K. L. STOLL.

CLINICAL MATERIAL ON PARTIAL PENETRATING CORNEAL TRANSPLANTATION. N. MEDVEDIEV and L. SATZ, Vestnik oftal. **15:** 7, 1939.

Twenty-two corneal transplantations were performed in the ophthalmic clinic of the Donetz Medical Institute during the years 1935 to 1937. In 13 of the eyes total leukoma and in 7 partial leukoma was present; in 6 eyes the leukoma was ectatic, and in 9 it was heavily vascularized. A von Hippel trephine was used, and the transplant was kept in place by egg membrane and crossed or straight sutures. The cornea from living persons was used in the majority of the cases; the eye was conserved in the citrated blood of the donor. In 19 cases vascularization of the transplant occurred in from four to twenty-two days after the operation, and in 4 cases glaucoma set in.

The result was poor, as in only 1 eye was fair improvement of vision obtained; there was slight improvement of vision in 6 cases, while in the others vision was either unchanged or worse than before the operation. These poor results are to be explained by the unfavorable material for transplantation.

O. SITCHEVSKA.

Experimental Pathology

THE PATHOGENESIS OF PHLYCTENAE: AN EXPERIMENTAL STUDY. A. KATSNELSON, Z. KACHAN and N. YUFA, Vestnik oftal. **15:** 3, 1939.

The authors attempted to establish the value of the pathogenetic disturbance of the carbohydrate metabolism and the tuberculous allergic diseases of the eye by both experimental and clinical observations (the latter data will be published later).

A 20 per cent solution of sodium lactate was introduced into the stomach of each of 45 rabbits (2 cc. per kilogram of body weight) and was followed by instillation of 1 drop of undiluted tuberculin into the conjunctival sac. Part of the animals were previously infected with tuberculous emulsion into the ear vein. A Mantoux test was done three to four weeks later. The blood was examined for sugar and for lactic acid, the first by the Hagedorn-Jensen method and the second by Furtsharnach's method. The eyes were desensitized by instilling 1 drop of a 1:1,000 dilution of tuberculin; if there was no reaction, stronger dilutions were used until tuberculin of full strength could be used. The experiment was divided into several series. These experiments showed that sodium lactate increased the reactivity of the infected rabbit to the extent that the latent sensitized conjunctiva reacted by a local inflammation because of the disturbance of carbohydrate metabolism. There was a flare-up of the tuberculous-allergic process in the eye without the local action of an antigen.

The article is long and lends itself to abstracting with difficulty. It is illustrated with several tables. The conclusions are as follows:

1. The introduction of sodium lactate causes in animals a hyperergic inflammation in conjunctivas previously desensitized to tuberculin as a response to local instillation of tuberculin.

2. The same amount of sodium lactate causes a spontaneous inflammatory reaction of the conjunctiva in tuberculosis-sensitized animals in the absence of local application of an allergen.

3. In healthy, nonsensitized animals with hyperlacticemia the tuberculin causes a transitory reaction in the eye.

4. In the majority of the cases the hyperergic reaction of the conjunctiva is accompanied by hyperlacticemia. The blood sugar is not perceptibly increased.

5. These experiments confirm the clinical observations of the relation of the ophthalmic reaction, the appearance of phlyctenae in subjects overfed with carbohydrates; the biochemical findings also confirm that lactic acid stimulates the reaction and is not consequent to it.

6. The role of carbohydrate metabolism, particularly that of lactic acid in the pathogenesis of tuberculous allergic diseases of the eye, should be considered in the course of desensitizing therapy in phlyctenar keratoconjunctivitis.

O. SITCHEVSKA.

General Diseases

GUMMA OF THE LIDS AND CONJUNCTIVA. A. LIPOVSKAYA, Vestnik oftal. **15:** 88, 1939.

That gummatous conditions of the lid and conjunctiva are rare is indicated by the fact that during a period of twenty-six years only 8 with such conditions were observed among 219,139 patients. Reports are given of 3 patients seen within a short period in 1936 in the university eye clinic of Kuban (Caucasus).

CASE 1.—A man aged 47 had an ulcerated lesion on the conjunctiva of the upper lid of the left eye which was diagnosed as tubercle of the conjunctiva because of the appearance and because of the history of

recurrent pleurisy and pneumonia. After the Wassermann reaction of the blood was found to be positive, he was given antisyphilitic treatment, and the ulcer on the conjunctiva and a similar one on the shoulder healed, leaving a scar, so that the diagnosis was changed to a gumma of the conjunctiva.

CASE 2.—A woman 37 years old complained of a persistent "stye" of the lower lid of the left eye for several months. The margin of the lid was ulcerated and the lid swollen. The condition could be taken for either an epithelioma or a tuberculous lesion. The Wassermann reaction of the blood was positive, and the ulcer healed after one course of antisyphilitic treatment. The character of the ulcer indicated tertiary syphilis.

The third case was interesting because interstitial keratitis developed in addition to the cutaneous lesion in the region of the brow, both conditions being part of tertiary syphilis. Since interstitial keratitis developed later in the other eye, the disease was evidently congenital syphilis.

O. SITCHEVSKA.

Lens

POST-CATARACT HYPHAEMA. A. S. PHILPS, Brit. J. Ophth. **24:** 122 (March) 1940.

The author gives the following summary of his paper:

"In 374 consecutive extractions there occurred 49 hyphaemata, giving a percentage of 13.13.

"Of these, 42 came from the section (85 per cent), and the remainder from the iris and conjunctival flap.

"In those that came from the section the average day of occurrence was 37 days after the operation, and they took 18.4 days to absorb.

"The type of operation has no influence on the incidence of hyphaema.

"No general condition such as diabetes or hyperpieses has any influence in their occurrence.

"It is due to local trauma such as squeezing the lids, which causes separation of the wound edges and rupture of the young vessels in the section.

"They can be prevented by the use of a corneo-scleral stitch.

"Several factors are enumerated which cause delay in absorption of the blood.

"The literature is reviewed, and though there is some difference of opinion, most of the younger authors think that they come from the section.

"The aqueous humour has no action on red cells, but can dissolve fibrin from the clot.

"The cells are absorbed by the iris, and do not enter the canal of Schlemm."

W. ZENTMAYER.

Lids

RADIUM IN THE TREATMENT OF CHALAZION. G. DVORAK-THEOBALD and C. J. WHITE, Am. J. Ophth. **22:** 750 (July) 1939.

The authors discuss irradiation of inflammatory conditions as compared with irradiation of tumors. They refer to the use of radium in ophthalmologic practice and briefly discuss the literature. A case is

reported; the data on 28 cases of chalazion treated with radium are given, and the manner of use of the substance is described. This treatment is suggested for cases in which operation is difficult or leaves an unsightly scar. The danger of radium therapy properly used is minimal.

W. S. REESE.

ISOLATED RHEUMATIC NODULE OF THE UPPER EYELID. J. S. GUYTON and J. M. MCLEAN, Am. J. Ophth. **22**:985 (Sept.) 1939.

Guyton and McLean report 2 cases of nodule of the upper lid. They give the following summary and conclusions:

"Two cases are reported in Negro children, both of whom show isolated subcutaneous nodular inflammatory tumors, in the region of the upper lid and brow, of the histologic nature of 'rheumatic' nodules. As the review of the literature indicates, such nodules may be: (1) the sole manifestation of rheumatic fever, (2) a form of either syphilis or yaws, (3) an accompaniment of rheumatoid arthritis, or (4) a subcutaneous form of granuloma annulare. Since all but the first and last possibilities can be definitely ruled out in our cases, we are forced to conclude that they represent either a manifestation of rheumatic fever or the subcutaneous variety of granuloma annulare—which, after all, may be one and the same thing."

W. S. REESE.

Neurology

DURAL HEADACHE AND INNERVATION OF THE DURA MATER. W. PENFIELD and F. MCNAUGHTON, Arch. Neurol. & Psychiat. **44**: 43 (July) 1940.

This study is concerned primarily with the nerve supply and pain reference of the dura mater in man and in the monkey. It is illustrated by clinical cases which cast light on dural sensitivity and on the radical treatment of falcial cicatrix, migraine and other forms of headache. The examples of referred pain to the eye from remote disturbance in the dura mater are interesting.

R. IRVINE.

DISEASES OF THE OPTIC DISK IN SEROUS MENINGITIS. V. RUB, Vestnik oftal. **15**: 77, 1939.

Five cases of serous meningitis with involvement of the optic disk are reported. In 1 of these the condition was descending optic neuritis, in 1 choked disk and in 3 atrophy of the optic nerve. In 4 cases the treatment with repeated lumbar punctures (with five to eight day intervals) gave strikingly good results, as the vision was improved from ability to count fingers to normal. In the fifth case, in which the atrophy of the optic nerve was of eighteen months' standing, with marked limitation of the visual field, the treatment was of no avail. The ages of the patients varied from 11 to 19 years.

Rub arrived at the following conclusions:

1. The optic nerve is frequently affected in patients with serous meningitis in the form of optic neuritis, choked disk and atrophy of the optic nerve.

2. Lumbar puncture is a valuable measure in the diagnosis of the diseases of the optic nerve.

3. Early systematic lumbar puncture is a good therapeutic agent in the control of the diseases of the optic nerve in patients with serous meningitis.

4. In untreated patients in late stages of the disease the lumbar puncture may not give the desirable therapeutic effect.

O. SITCHEVSKA.

Ocular Muscles

MYOSITIS OF PERIOCULAR MUSCLES. D. MICHAIL and LAVINIA RUSU, Ann. d'ocul. **177:** 97 (March) 1940.

Myositis of the external muscles of the eye has been described in some articles and special communications, especially in connection with the pathology of the orbit, in which the question of exophthalmos has been taken up.

This article is divided into two parts. In the first part primary myositis of the periocular muscles is taken up, and afterward secondary myositis is discussed. The first form is rare, only a few cases up to the present having been reported; the writer adds 2 cases of his own. The condition is often due to syphilis, and on account of the intolerable pain enucleation is required. Roentgen treatment has had some effect. The 2 cases of the author are given in considerable detail.

Regarding the secondary form, the first place in the causation is given to syphilis. The condition may also be caused by tuberculosis, ophthalmic thrombophlebitis, foreign bodies, inflammations of the orbital cellular adipose tissue and tenonitis. Among the ocular causes are suppurative panophthalmitis, perforating wounds of the globe and atrophic globes. Three cases of the secondary form are reported in detail. There are two illustrations, four microscopic figures and a bibliography.

S. H. MCKEE.

THE RIDDLE OF AMBLYOPIA EX ANOPSIA. A. VOGT, Klin. Monatsbl. f. Augenh. **103:** 293 (Sept.) 1939.

Satisfactory explanations of the origin and existence of amblyopia ex anopsia have not been given in textbooks. The weak eye appears as normal ophthalmoscopically and anatomically as the normal eye. Observing that the central vision of the weak eye decreases rather quickly, one must consider that central and peripheral vision have different cerebral origins. For this reason the outline of the field of vision is normal in the weak eye. Early operation and early visual exercise will bring back the activity of the macula. This and other facts are proof that amblyopia is due to lack of visual exercise in earliest childhood. Vogt places the seat of unilateral amblyopia ex anopsia in the brain and not in the eyeball for the following reasons: Color sense and light sense of the entire retina are preserved in the amblyopic eye, which is antomically and ophthalmoscopically intact. The possibility of improving the vision in the amblyopic eye is proof of the presence of a "functional sleep" of the macula and of intactness of the retina as the perceiving organ. The absence of

hemianopic disturbances is explained by double supply to the macula. The cerebral seat of amblyopia is evidenced, furthermore, by the experience that bilateral congenital blindness, e. g., in cases of congenital cataract, may be cured by later operations. Analogous conditions of "functional sleep" of important cerebral activity may be found in the speech centers of the brain. Destruction of the functioning side will awaken the symmetric center of the opposite side, stimulating its faculty of speech. In the same manner occlusion of the central vein of a visually perfect eye will force an extremely amblyopic eye to resume visual function. Vogt referred to a case in which useful macular vision returned notwithstanding the patient's age of 44 years. K. L. STOLL.

Retina and Optic Nerve

MACULAR LESIONS IN THE YOUNG. E. REDSLOB, Ann. d'ocul. **176:** 738 (Oct.) 1939.

Macular alteration in older persons is an everyday occurrence and is attributed to a wearing out of the retinal tissue from vascular disease. Bailliart pointed out that macular lesions in young persons are much less frequent and therefore less known. Most textbooks classify these cases as familial macular degenerations of the Stargardt or Behr type or as a complication of idiocy, such as the infantile type of Tay-Sachs or the juvenile type of Spielmeyer-Stock.

Characteristic points of such macular lesions are: the familial and hereditary character, (2) an almost absolute analogy in the evolution of the disease, (3) bilaterality and (4) complete agreement between the subjective and the objective signs. Hereditary degenerations show themselves first between the sixth and the eighth year, again at 14 and at 20 years and finally at old age, that is to say, at the periods when the most manifest changes take place in the body development. In each family reported by Behr the condition developed at the same ages—childhood, adolescence and old age.

The author has often observed hemorrhages in the macular area of young persons from 9 to 27 years of age. The cause of these is not known. They are encountered in persons who are otherwise perfectly normal but who present a certain fragility of the vessels. These hemorrhages are not destructive, do not cause much dimness of vision and do not provoke a central scotoma. They have been often observed in patients coming for examination of refraction. These lesions have no connection with the macular hereditary degeneration of Behr or with the cystic degeneration of Vogt. S. H. MCKEE.

ALTERATIONS IN THE RETINA OBSERVED DURING THE COURSE OF CHRONIC NEPHRITIS. HENRY LAGRANGE, Ann. d'ocul. **176:** 785 (Nov.) 1939.

This essay on pathogenic classification, in response to numerous interesting articles, calls particular attention to the role of arterial hypertension, formerly "angiopathic albuminuric retinitis," in the genesis of alterations in the retina observed in the course of nephritis.

The author divides the material of his essay into clinical facts, pathogenesis and diagnosis. Under clinical facts he discusses primary retinal infiltrations, consisting of the chalk-white, powder-like stellate and purpuric types; the lesions of hemorrhagic retinitis, and edema of the retina. Under pathogenesis, he takes up angiopathy, hypercholesteremia, retention of urea and coincidence of uremia and primary infiltration, including the chalk-white, powder-like and purpuric lesions of the retina.

In his summary, the writer states that the distinct features of disturbances of renal function that can be seen ophthalmoscopically are: (*a*) the primary, white powder-like infiltration of the retina, usually associated with the secondary anemia of nephritis, and the purpuric, discrete, flame-like extravasations of blood, characteristic of a pathologic diapedesis through the arterioles, regulated by a fleeting recurrent process or a progressive process, the existence of which is explained on the basis of toxic retention; (*b*) angiopathic signs, varying from massive hemorrhages that are a part of the manifestation of permanent arterial hypertension of nephritic origin to manifestations of malignant hypertension and arteriosclerosis, and (*c*) phenomena of papilledema that arise from one or the other of two mechanisms, that is, trophic edema associated with vascular exudation and edema due to increased pressure of the cerebrospinal fluid.

The disturbances of the visual function attributable to the clinical forms of chronic nephritis cannot be compared with the etiologic classification, the old or new clinical anatomic classification or the syndrome of renal insufficiency. They are strictly related to the local mechanisms which control them, which the author has indicated as the mechanism that causes the early and purpuric white powder-like infiltrations, which can only effect at first a moderate functional disturbance in spite of their abundance and their macular localization, and that which differentiates the latter from the hemorrhages of hypertension, which are expressed on the contrary violently as soon as the retinal trophic edema and mechanical edema (stasis of the hypertension of the cerebrospinal fluid), which are slow in giving rise to functional manifestations and which must be differentiated from cerebral edema responsible for the amaurotic hemianopic phenomena related to the generalized edemas and often like them, variable, fleeting and recurrent. S. H. McKee.

Changes in the Retina Due to Loss of Blood and the Effect of Blood Transfusion. P. Batarchukoff, Vestnik oftal. **15:** 23, 1939.

A woman aged 33 complained of sudden impairment of vision which occurred three weeks previously; two days before that she had had a curettage because of a febrile abortion and uterine bleeding for two weeks preceding the operation.

The clinical diagnosis was bilateral ischemia and angiospasm of the retina due to metrorrhagia and abortion. There was marked edema of the retina at the macular region and about the disk, and the arteries were constricted. There was a defect of the right lower visual field, and in the left eye only the upper part of the temporal quadrant of the field was present. Examination of the blood revealed 40 per cent hemoglobin,

a color index of 0.69 and a greatly diminished number of the erythrocytes with typical anemic changes in them. A blood transfusion was given in ten days because there was no improvement with ordinary measures.

The diagnosis of functional angiospasm was made because of the evenly distributed narrowing of the retinal blood vessels and because of the presence of a Salus 2 sign. The hemianopia of the lower half of the visual field was evidently due to the fact that when a considerable amount of blood is lost there is more blood in the lower half of the retina (according to the law of gravitation), so that the vessels are more protected from spasm than those of the upper half of the retina.

Batarchukoff states the belief that the spasm of the retinal vessels and ensuing complications are due to a deficiency of oxygen. The striking therapeutic result of the single blood transfusion in this case suggests the advisability of prophylactic blood transfusions in any case of great loss of blood, in order to prevent ocular complications.

O. SITCHEVSKA.

Tumors

TUMORS OF THE ORBIT. A. I. POKROVSKY, Vestnik oftal. **15:** 146, 1939.

Three cases of mixed tumor of the lacrimal gland are reported, the patients being 17, 32 and 45 years of age respectively. The tumors were of slow growth, freely movable and of firm consistency. Exophthalmos was present in each case. No recurrences were observed after complete removal of the tumors in the capsule.

The main histologic changes were as follows: 1. There was a variety of forms of epithelial clusters, starting from atypical lobules of the lacrimal gland tubular epithelial cells, with a transition to solid bands of epithelial cells between the pronounced stroma and netlike bands of cells; massive cellular clumps were also present. 2. The stroma of the tumor varied as to its volume and pathologic changes (mucus and hyaline degeneration, resembling the cartilage of the structure).

Pokrovsky gives a detailed review of the literature and discusses the pathogenesis and character of mixed tumors. He believes that they should be called benign "epitheliomas" of the lacrimal glands because of their benign clinical course. Since they may become malignant at some time, the treatment should consist of an early complete removal of the tumor without injury to the capsule. If an orbitotomy presents difficulties in removing the tumor in toto, the Krönlein operation should be resorted to. The patient should be observed in order to remove early any recurrent growth.

O. SITCHEVSKA.

Book Reviews

Text-Book of Ophthalmology. By Sir W. Stewart Duke-Elder. Volume 3. Diseases of the Inner Eye. Price, $18.50. Pp. 1,373, with 1,400 illustrations, including 164 in color. St. Louis: The C. V. Mosby Co., 1941.

The much awaited third volume of Duke-Elder's textbook has just appeared, notwithstanding the tragic experiences which the English are passing through at this time. In this volume the diseases of the inner eye are taken up, and the subject matter is considered under the following headings: uveal tract, 436 pages; retina, 383 pages; optic nerve, 175 pages; lens, 142 pages; vitreous body, 34 pages; anomalies of intraocular pressure, 150 pages, and intraocular parasites, 21 pages. As in the preceding volumes, each section is introduced by a portrait and a short biographic sketch of a famous person in ophthalmology associated with progress in the subject under consideration.

Each subject is illustrated by microscopic slides of the histologic picture when available, by macroscopic drawings of the lesion and by the ophthalmoscopic picture in black and white or in colors, and at the end of each chapter there is a list of bibliographic references.

The chapter on diseases of the uvea begins with a discussion of hemorrhages and includes a description of disciform degeneration of the macula (senile and juvenile). Endogenous infection of the uvea, according to the author, is due presumably to organismal allergy or toxic influence. In cases of focal infection the condition is of an allergic nature rather than directly infective (p. 2141) or is due to excitation of a local allergic reaction in an immune but allergic patient (p. 2143). Tuberculosis of the uvea is an allergic reaction arising from glandular lesions (p. 2147). Sympathetic ophthalmitis is almost certain to be infective in origin (p. 2335), and an unknown virus, probably inhabiting the conjunctival sac, is the most attractive hypothesis.

The section on diseases of the retina brings the portraits of Marcus Gunn and George Coats. The subject is divided into chapters on general considerations, disturbances of circulation, retinitis, retinopathies associated with general diseases, cysts, tumors and detachment of the retina. In the last-mentioned chapter is a photograph of Gonin. The clinical types of retinal detachment are carefully described, and the theories of its cause are elucidated. The methods of treatment are given, with a most instructive description of the resulting pathologic changes.

The chapter on diseases of the optic nerve brings the portrait of George de Schweinitz. This subject is introduced with a consideration of the finer anatomy of the optic nerve, and the subject is treated under the following headings: disturbances of the circulation (which includes papilledema), inflammation of the optic nerve (optic neuritis), toxic amblyopia, specific infections (tuberculosis and syphilis), degenerations (vascular), atrophy of the optic nerve and tumors. It is well illustrated with excellent drawings of macroscopic and microscopic lesions.

The next chapter discusses diseases of the lens. The author states that a considerable amount of information on the chemical changes which the lens undergoes in the development of cataract has been accumulated, and though no definite clues as to the causes of cataract have been presented, this information is not without promise (p. 3118). A summary of the chemical changes occurring in cataract is to be found on page 3125 and of the metabolic features in the development of cataract on page 3135.

An excellent description of the diseases of the vitreous follows, and the volume concludes with the important chapter on glaucoma, bringing the pictures of Priestly Smith and F. Lagrange. Secondary glaucoma is first treated. The author believes that glaucoma following central retinal vein thrombosis is due to blockage of the filtration angle in which a chronic state of stasis and congestion is brought about by degenerative and toxic products. Primary glaucoma is probably the local expression of general systemic pathologic or degenerative processes. He (p. 3339) concludes that primary glaucoma tends to occur in persons over middle age who have some vascular disability, either of sclerosis (degeneration) or of dysfunction (vasomotor or endothelial instability), bound up with imbalance in the neurovegetative and endocrine systems. On page 3362 Duke-Elder summarizes his position on the etiology of primary glaucoma and concludes by stating that "no one can complain however of the variety, the scope, the interest or the difficulty of the problems awaiting future research." This chapter on glaucoma is an unusually sensible and admirable description of this baffling disease and cannot be praised too warmly.

This volume is encyclopedic in character, was written by a master mind, is a mine of information, and exhaustive study most complete in every detail and admirable in value and contains much information assayed with rare critical and scientific judgment. One must express the greatest admiration for the author's stupendous industry, and the thanks of all ophthalmologists go to him for the assembly of this mass of information, which will be of the greatest help to every earnest student of ophthalmology. The printing and the illustrations are of the best, but if a small criticism be permitted, it is that this volume is so large and heavy as to be unwieldy.

ARNOLD KNAPP.

Surgical Anatomy of the Head and Neck. By John Finch Barnhill, Miami Beach, Fla. Second edition. Rearranged and revised. Price, $15. Pp. 773, with many illustrations. Baltimore: The Williams & Wilkins Company, 1940.

The surgical anatomy of the orbit is presented by Barnhill in his new book, which is in the form of a dissection manual. The student is directed to examine the skull and note the important bony landmarks of the orbit. Directions are then given for a dissection of the orbit from above, calling attention especially to the periorbita, the frontal and trochlear nerves, the orbital fat, the extraocular muscles, the ophthalmic artery and veins, the ciliary ganglion, the lacrimal gland, Tenon's capsule and the optic nerve. The danger of infection of the orbit from the accessory nasal sinuses is stressed, and the possibility of retrobulbar neuritis

developing from an infection of the sphenoid sinus is mentioned. He calls attention to the danger of diplopia following a radical operation on the frontal sinus (Killean, Lynch and Sewell) and stresses the need for careful replacement of the periosteum and the superior oblique pulley after these operations. Also, mention is made of the danger of cavernous sinus thrombosis following infection of the face.

There are some minor errors present, which may be briefly noted. The short ciliary nerves are stated to be motor, whereas most authorities agree that these are mixed nerves carrying sympathetic and sensory, as well as motor, fibers to the globe. The long ciliary nerves are said to be branches of the third nerve, to cause constriction of the pupil and to be postganglionic from the ciliary ganglion. According to Whitnall, the long ciliary nerves are derived from the nasociliary nerve, a branch of the first division of the fifth nerve, and carry only sensory impulses together with a few sympathetic fibers to the iris for dilation of the pupil. These fibers do not come from the ciliary ganglion and do not cause constriction of the pupil. In figure 210 one nerve (no. 6) is labeled the "great deep petrosal nerve," and it should read "sympathetic root of the ciliary ganglion," since it runs from the carotid sympathetic plexis to the ciliary ganglion. This is an obvious clerical error since the location of these two nerves is accurately described in the text.

Most ophthalmologists would hesitate to agree with the author's conception of an episcleral space and of Tenon's capsule. The latter is described as being so thick and resisting as to not collapse after the eyeball is taken out.

The text is intended primarily for otolaryngologists, whose interest in the orbit certainly is not as meticulous as that of the ophthalmologist. For the otolaryngologist Dr. Barnhill's chapter on the anatomy of the orbit is a valuable contribution, but for the ophthalmologist much which is important surgically has been necessarily omitted.

RAYNOLD N. BERKE.

The Anatomy of the Eye and Orbit. By Eugene Wolff, London. Second edition. Price, $7.50. Pp. 374, with 242 illustrations. Philadelphia: The Blakiston Company, 1940.

This book was favorably reviewed in the ARCHIVES (**10: 723** [Nov.] 1933) after its publication. The second edition now appears with several corrections and the addition of 60 illustrations, most of which have been prepared by the author in the pathologic laboratory of the Royal Westminster Ophthalmic Hospital. These include flat sections of the retina. The section on the blood supply of the visual pathways has been rewritten. There is a note on the differential staining of the rods and cones and on the structure of the iris.

The new additions enhance the value of the book, which is already noted for the lucidity of the text, the clearness and excellence of the illustrations and the frequent references to practical ophthalmologic principles. Wolff's book is an important contribution to scientific ophthalmology and belongs on every ophthalmologist's book shelf.

ARNOLD KNAPP.

Thirteenth Annual Report of the Memorial Ophthalmic Laboratory, Giza, Cairo, 1938. Ministry of Public Health. Paper. Price, P. T. 35. Pp. 137. Illustrated. Cairo: Schindler's Press, 1940.

The report covers in detail the activities of the laboratory for the year 1938 and offers a wealth of interesting case reports illustrated by photographs and drawings, some of which are in color. The cases are examples of such conditions as lipoid degeneration of the cornea and of the palpebral conjunctiva, episcleral abscess, bilateral inflammatory pseudotumor of the orbit, leproma of the limbus, adenoid epithelioma of the eyelid, bilharzial granuloma of the bulbar conjunctiva and adenocarcinoma of the lacrimal gland.

Mention is made of the occurrence of small xerotic patches on the bulbar conjunctivas of 2 young adults with advanced pellagra. In 30 cases of pellagra of long duration in adults who had been previously examined by El-Tobgy, nothing abnormal was found in the eyes except senile cataract in 2 instances.

The efficacy of sulfanilamide and its derivatives in the treatment of gonococcic ophthalmia and trachomatous keratitis is also noted. It is stated, however, that the drugs had only moderate effect on the conjunctival lesions of trachoma of stages 1 and 2, which is probably explained, in the reviewer's opinion, by the apparent failure to follow the cases for a sufficient period after completion of treatment. It is now well recognized that absorption of follicular and papillary hypertrophy in cases of trachoma may continue for as long as two months after treatment.

The sulfanilamide products are reported as having little or no effect on conjunctivitis caused by the Koch-Weeks bacillus.

The research section includes a report by Bland of certain attempts, thus far unsuccessful, to cultivate trachoma virus in tissue culture. Lyons has continued his studies on vernal catarrh with particular reference to possible endocrine factors. Kamel concludes the section with a detailed and important study of ophthalmomyiasis based on 32 cases observed in various parts of Egypt. Most of the patients were from the lower part of Egypt, and in all of them the condition was caused by Wohlfahrtia magnifica. The majority of cases occurred in July, August and September.

PHILLIPS THYGESON.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Albert C. Snell, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. F. P. Calhoun, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va. Time: May 29-31, 1941.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Wisconsin Rapids. Time: June 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Franklin P. Maury, Professional Bldg., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. W. E. McClellan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.
Place: Macon. Time: May 13-17, 1941.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.
Place: Atlantic City. Time: June 3-5, 1941.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. W. Carpenter, 200 E. North St., Greenville.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
Place: San Antonio. Time: December 1941.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 628 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Richard Gamble, 30 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Harold Mulligan, 1680 N. Vine St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Morris Davidson, 80 Centre St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. Howard Heine, 635 N. Main St., Fremont, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 5 p. m., Jan. 22. 1941.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.